An open labeled randomized controlled trial comparing costs and clinical outcomes of open endotracheal suctioning with closed endotracheal suctioning in mechanically ventilated medical intensive care patients.

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE RULES AND REGULATIONS FOR THE MD BRANCH I, GENERAL MEDICINE EXAMINATION OF THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY, TO BE HELD IN MARCH 2009.

C E R T I F I C A T E

This is to certify that the dissertation entitled `**An open labelled randomised controlled trial comparing costs and clinical outcomes of open endotracheal suctioning with closed endotracheal suctioning in mechanically ventilated medical intensive care patients'** *is* the bonafide original work of Dr. Deepu David, towards the M.D. Branch-I (General Medicine) Degree Examination of the Tamil Nadu Dr. M.G.R University, Chennai, to be conducted in March, 2009.

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C E R T I F I C A T E

This is to certify that the dissertation entitled `**AN OPEN LABELLED RANDOMISED CONTROLLED TRIAL COMPARING COSTS AND CLINICAL OUTCOMES OF OPEN ENDOTRACHEAL SUCTIONING WITH CLOSED ENDOTRACHEAL SUCTIONING IN MECHANICALLY VENTILATED MEDICAL INTENSIVE CARE PATIENTS'** is the bonafide original work of Dr. Deepu David, towards the M.D. Branch-I (General Medicine) Degree Examination of the Tamil Nadu Dr. M.G.R University, Chennai, to be conducted in March, 2009.

Signature of the guide

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CONTENTS.

INTRODUCTION.

India is a vast nation with the varied forms of health care problems of a developing country. The major medical problems include malnutrition and infections. Hence, less importance had been given to the specialty of critical care and the need is only recently being recognized. Although the technologic and scientific advances occur at a rapid rate in developed countries, these advances are variable in developing countries(1). With managed care and escalating health care spending even in an affluent society, measures to curtail spending are being implemented. With this in mind, developing countries with more basic health care needs have to prioritize their resources(1). Philosophically and economically, however, the impact of an untimely demise of the bread-winner from acute myocardial infarction or acute respiratory distress syndrome (ARDS) can be very devastating, particularly in developing countries with poor social security benefits. Furthermore, the prevalence of diseases that are reversible with intensive supportive care, such as those due to overdoses and infections, makes the role of intensive care units(ICUs) a necessity in every part of the world(1). The cost of ICU care per day in a tertiary care center in India (in 1991) was reported to be Rs 3200 per patient ($167.70). Staffing, intravenous fluids, and drugs accounted for 75% of the cost of ICU care, whereas 15% accounted for laboratory investigations and 6.9% for disposables(1, 2).Whereas a study done in a medical ICU in a developed country showed the median cost per day during the same time period(1991) to be $1,357(3), almost seven times the cost in an ICU of a developing country. Hence the aim of a intensivist in a developing country should be to give the maximum effective care keeping in mind the limited resources available. The reason behind this study was to compare the cost

effectiveness of two suctioning systems and also to compare the incidence of ventilator associated pneumonia between the suctioning systems.

Nosocomial infections (NIs) now concern 5 to 15% of hospitalized patients and can lead to complications in 25 to 33% of those patients admitted to ICUs(4). They are viewed as an inexorable tribute to pay to the more aggressive management of the population, characterized by the use of sophisticated technologies and invasive devices. The pathophysiology of NIs includes colonization of the host by potentially dangerous pathogens, such as microorganisms from exogenous or endogenous sources, including resistant strains such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), azole-resistant Candida spp, and extended-spectrum ß-lactamase (ESBL) Gram-negative pathogens. Ventilator-associated pneumonia, catheter-related bloodstream infections, surgical site infections (SSIs), and urinary catheter-related infections account for > 80% of NIs.(5, 6)

The Study on the Efficacy of Nosocomial Infection Control (7-9)from the CDC has suggested that at least one third of NIs are preventable through infection control programs, which have been implemented in most centers during the last 2 decades. Risk factors are well-identified and have been the target of efficient preventive measures.Several measures have been proposed to reduce the nosocomial infections and cross infections in ICU,taking into consideration the costs involved by adopting such measures and also their benefits and harms.

It has been suggested that closed endotracheal suctioning (CES) should reduce the risk of ventilator-associated pneumonia (VAP) by eliminating environmental contamination of the catheter before introduction into the endotracheal

tube (ETT). Another benefit of CES, often overlooked, is the limitation of aerosolization of infectious mucus particles. Thus, CES potentially has a role in preventing the spread of infection between patients and from patients to clinical staff (10). In recent years, there has been a global trend in ICUs to change from the established system of open endotracheal suctioning (OES) to the newer (and more costly) closed-suctioning systems(11). However, these potential advantages have not been shown to translate into clinically meaningful improvements, with several recent meta-analyses(12-14) having reproducibly demonstrated no benefit of CES over OES for a number of outcome measures, including incidence of VAP, mortality and length of ICU stay. These results are important for the implementation of evidence-based clinical practice but are not yet conclusive, considering that the meta-analyses themselves may have been underpowered to detect a true difference between suctioning systems(12). The majority of clinical trials included in the meta-analysis were conducted in first-world environments and it may, therefore, not be appropriate to directly apply these results to other ICU populations.

ICU's in the developed world, where adequate bed spacing is present and there are no constraints of staffing and sufficient resources, the choice of suctioning systems may be based on staff preference as well as ocuupational health issues(11). However, the debate is clearly still open when addressing the specific challenges faced in ICUs in developing countries- issues which may predispose to a particularly high incidence of nosocomial infection.. These include inadequate staffing, patient overcrowding, an increased burden of infectious diseases, and resource limitations. With the high incidence of infectious diseases such as pulmonary tuberculosis, the focus should perhaps be broadened from the individual patient to the

wider ICU population (including staff and other patients). If CES were to reduce the risk of infection to nursing staff and patients, it may be worth the extra cost of using the system. However, until objective clinical benefit has been demonstrated, the use of CES cannot be justified in developing nations(11).

Hence this study was done comparing costs and clinical outcomes of open endotracheal suctioning with closed endotracheal suctioning in mechanically ventilated medical intensive care patients. This study is proposed to answer the question of the utility as well as benefit of closed endotracheal suctioning in the intensive care environment in a developing country.

AIMS AND OBJECTIVES OF THE STUDY

Aim:

To compare the cost and clinical outcomes with the use of closed endotracheal suctioning, as compared to open endotracheal suctioning in the ICU setting of a tertiary care hospital.

Objectives:

To determine whether the use of closed endotracheal suctioning as compared to open endotracheal suctioning would result in

1. Lower costs of therapy (in this situation costs involved with suctioning).
2. A reduction in the incidence of ventilator associated pneumonia (VAP).
3. A similar incidence of left basal collapse determined radiologically.
4. Lower mortality.
5. A reduction in the duration and extent of desaturation.

REVIEW OF LITERATURE

Literature review structure

1) **Critical Care in India-a emerging speciality(12)**
2) **Endotracheal suctioning and different suctioning methods.(13)**
3) **Closed endotracheal suctiong systems.(13)**
4) **Advantages and disadvantages of different suctioning systems.(15)**
5) **Ventilator associated pneumonia.(16)**
6) **Type of suctioning and ventilator associated pneumonia.(36)**
7) **Type of suctioning and its effect on environmental contamination.(37)**
8) **Type of suctioning and its effect on ventilatory and hemodynamic parameters.(41)**
9) **Type of suctioning and cost effectiveness.(43)**
10) **Type of suctioning and nursing related outcomes.(45)**
11) **Metaanalysis comparining the open and closed suctioning systems.(46)**

CRITICAL CARE IN INDIA-AN EMERGING SPECIALITY

Critical care is still an emerging specialty in developing countries like India**.** India with over a billion population with majority living in villages is still deficient in critical care facilities with not enough penetration into the villages. The spectrum of diseases widely varies in developing countries as compared to developed countries**.** Fulminant infections and other problems peculiar to poor tropical developing countries form an extremely important group of patients necessitating critical care. What is more, intensive care in this group of patients is extremely rewarding, with severe tetanus being a classic example (1, 15). Thus, critical care units of large teaching hospitals and of district hospitals serving small towns and their adjacent villages deal with a higher proportion of patients with acute infections, trauma, poisoning, severe burns, and poisonous snake bites(1). Poisonings, in fact, form an extremely important cause of emergency admission to medical ICUs. Organophosphorus poisoning is one of the leading causes of suicide in India, and when managed well can give gratifying results. Hence any intervention or a procedure which would cut down ICU costs or reduce nosocomial infections would make ICU care more affordable(1).One such area would be endotracheal suctioning and prevention of ventilator associated pneumonia where much studies are not available from developing countries. A brief discussion about the endotracheal suctioning and ventilator associated pneumonia is given below.

ENDOTRACHEAL SUCTIONING AND DIFFERENT SUCTIONING METHODS.

Endotracheal suctioning is performed in intubated mechanically ventilated (MV) patients as a routine, essential part of care to clear endotracheal secretions.

Two methods of endotracheal suctioning are in practice –the open endotracheal suctioning (OES) system where suctioning is performed after disconnecting the respiratory circuits and using sterile single use suction catheters and the closed endotracheal suctioning (CES) system, where suctioning is performed without disconnecting the respiratory circuit, and uses multi-use in-line catheters that are enclosed in a sheath along with the respiratory circuit.

CLOSED ENDOTRACHEAL SUCTIONING SYSTEM.

Closed-circuit suction systems were introduced nearly 25 years ago as a method to reduce complications associated with the traditional suctioning procedure. CES device consists of a T-shaped suction union which incorporates a re-usable suction catheter. The catheter is withdrawn into a flexible plastic film sleeve between successive suction procedures which prevents contact between the catheter and the environment and permits the same suction device to remain in position in the breathing system before it is replaced. The tip of the catheter protrudes into the lumen of the catheter mount through a close-fitting flange. The catheter is grasped through its sleeve to advance it into the tracheal tube connector and on into the

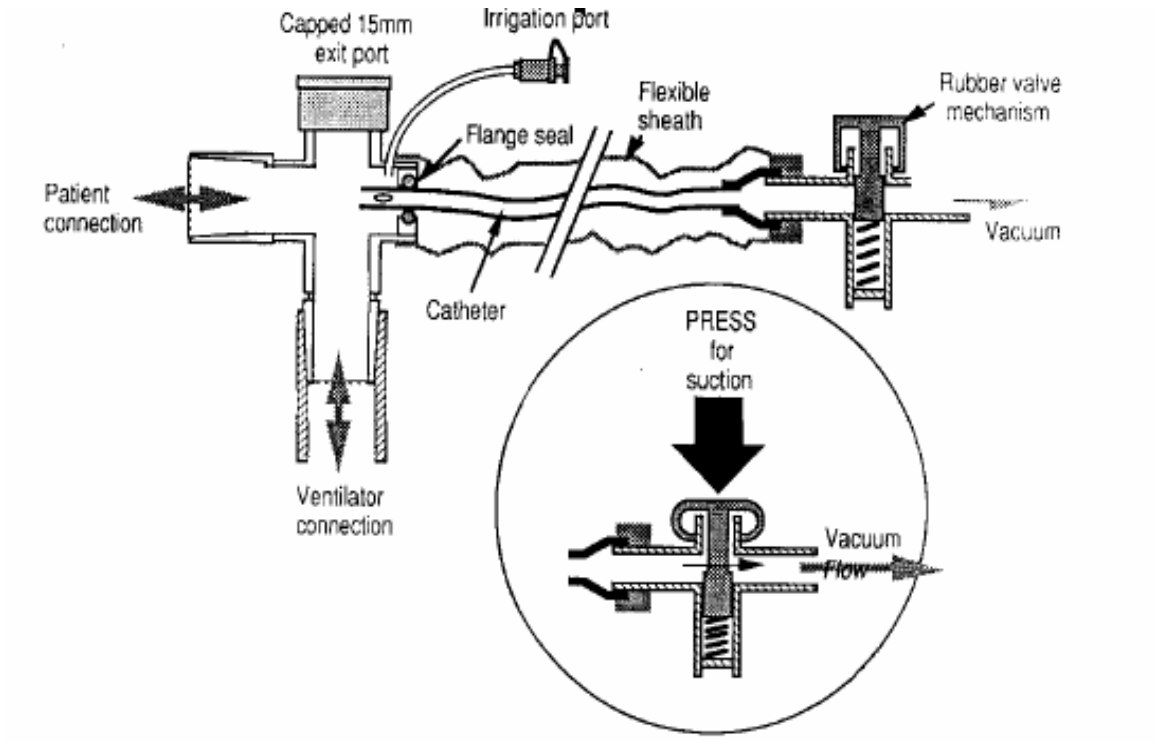

Figure 1:Example of a closed suction catheter(10).

tracheobronchial tree. The flange provides a gas-tight fit around the catheter and prevents the loose-fitting sleeve from being inflated during IPPV. It also wipes any secretions from the outer surface of the catheter as it is withdrawn. The catheter is fitted with a vacuum control valve which has a spring-based piston action. This device must be compressed continuously to maintain suction to prevent suction from being applied continuously to the airways inadvertently. The devices were provided with an irrigation port (with one way valve) on the catheter mount so that irrigation fluid could be instilled through the port. This fluid was aspirated through the catheter, by operating the suction valve, thereby washing it clear of accumulated secretions thus allowing lavage and irrigation without leakage of ventilation and secretions. It also maintains closed circuit during procedures such as fiberoptic bronchoscopy and mucus sampling.(Figure 1)

PROPOSED ADVANTAGES AND DISADVANTAGES OF DIFFERENT SUCTIONING SYSTEMS.

The purported advantages of closed-circuit suctioning include: no need to break the circuit; maintenance of ventilation, oxygenation, and positive end-expiratory pressure; and reduced environmental and caregiver contamination. This mode of suctioning has comparatively fewer physiological disturbances and consequences during suctioning(16, 17) as well as ease of use, given that only one operator is required for suctioning(18). Further, CES is postulated to reduce VAP rates by decreasing environmental contamination during suctioning (10).These potential advantages have led to the conduct of several randomized controlled trials (RCT) that compared CES and

OES. These individual trials failed to show a superiority of one type of suctioning over the other(12).

The disadvantages of CES include the risk of producing high negative pressures if the amount of air suctioned exceeds the gas flow delivered to the patient by the ventilator(19); reduced efficiency in clearing thick secretions from the airways(20);and the high financial cost of the system(21),which may have replaced daily in order to avoid microbial lower respiratory tract colonization(22).Practically, there is also a risk of not withdrawing the catheter completely after the suctioning event, thus partially occluding the ETT and increasing airway resistance. These disadvantages may actually favor the use of OES(11).

A recent meta-analysis performed in our institution(12)suggested the lack of superiority of open over closed suctioning. The authors however proposed that the studies that were included in the meta-analysis comprised of trials performed in the Western environment and hence could not be applied to our cohorts of patients in our country. Further they proposed that the meta-analysis was under powered to answer the question and that there were methodological weakness in the studies that limited generalizability to the average ICU patient(12).

VENTILATOR ASSOCIATED PNEUMONIA (VAP)

Ventilator-associated pneumonia(VAP) refers specifically to nosocomial bacterial pneumonia that has developed in patients who are receiving mechanical ventilation(23). VAP is defined as pneumonia occurring more than 48 hours after endotracheal intubation and initiation of mechanical ventilation.(24) Ventilator-associated

pneumonia that occurs within 48 to 72 hours after tracheal intubation is usually termed early-onset pneumonia; it often results from aspiration, which complicates the intubation process. Ventilator-associated pneumonia that occurs after this period is considered late-onset pneumonia.(23). Ventilator-associated pneumonia (VAP) is common in the intensive care unit (ICU), affecting 8 to 20% of ICU patients and upto 27% of mechanically ventilated patients(25).Early-onset ventilator-associated pneumonia is most often due to antibiotic-sensitive bacteria (eg;oxacicillin sensitive Staph Aureus,Haemophilus Influenzae and Streptococcus pneumoniae),whereas late-onset VAP is frequently caused by antibiotic-resistant pathogens (e.g., oxacillin-resistant Staph. aureus, Pseudomonas aeruginosa, acinetobacter species, and enterobacter species)(27-29). Microorganisms responsible for VAP may differ according to the population of patients in the ICU, the durations of hospital and ICU stays, and the specific diagnostic method(s) used. The high rate of respiratory infections due to GNB in this setting has been repeatedly documented(24).A study done in one of the tertiary hospitals in India also found gram negative organisms to be the main isolates from patients who developed Ventilator associated pneumonia(26).(Table 1)

Epidemiology of VAP.

VAP has an incidence ranging from 6.8% to 44% (18, 30-32)However some studies done in India showed incidence rates of 16.7%(33)and 47%(34)In contrast, Cook and coworkers demonstrated in a large series of 1,014 mechanically ventilated

	On ventilator (n=121)	Off ventilator (n=9)
Microorganisms	n (%)	n (%)
Gram-negative bacteria	377 (93.3)	2 (13.3)
Pseudomonas aeruginosa	141 (34.9)	1 (6.6)
Escherichia coli	72 (17.8)	1 (6.6)
Klebsiella pneumoniae	69 (16.8)	-
Acinetobacter spp	58 (17)	-
Citrobacter spp	27 (6.6)	-
Enterobacter spp	5 (1.2)	-
Proteus vulgaris	5 (1.2)	-
Gram-positive cocci	27 (6.6)	13 (86.6)
MRSA	14 (3.4)	8 (53.3)
MSSA	10 (2.4)	5 (33.3)
Enterococcus spp	3 (0.7)	-
Polymicrobial	68 (16.3)	2 (13.3)
Total isolates (426)*	404 (94.8)	15 (3.52)

*Nocardia spp and 5 Corynebacteria spp. isolated
(They make total isolates on ventilator = 410 and off ventilator = 16)
MRSA, Methicillin-resistant *Staphylococcus aureus*
MSSA, Methicillin-sensitive *Staphylococcus aureus*

Table 1- Etiology of ventilator associated pneumonia from a study done in a tertiary care centre in India(26).

patients that, although the cumulative risk for developing VAP increased over time, the daily hazard rate decreased after Day 5 (35).The risk of VAP is highest early in the course of hospital stay, and is estimated to be 3%/day during the first 5 days of ventilation, 2%/day during Days 5 to 10 of ventilation, and 1%/day after this (35). Early-onset VAP, defined as occurring within the first 4 days of hospitalization, usually carry a better prognosis, and are more likely to be caused by antibiotic-sensitive bacteria. Late-onset VAP (5 days or more) are more likely to be caused by multidrug-resistant (MDR) pathogens, and are associated with increased patient mortality and morbidity(25). However, patients with early-onset HAP who have received prior antibiotics or who have had prior hospitalization within the past 90 days are at greater risk for colonization and infection with MDR pathogens and should be treated similar to patients with late-onset or VAP(Table 2).(36)

Nosocomial pneumonia is a leading cause of death from hospital-acquired infections, with an associated crude mortality rate of approximately 30 percent(37). The incidence of VAP-attributable mortality is difficult to quantify due to the possible confounding effect of associated conditions, but VAP is thought to increase the mortality of the underlying disease by about 30% (37).Mortality rates in patients with VAP range from 20 to 50% and may reach more than 70% when the infection is caused by multi-resistant and invasive pathogens (34, 37, 38). It has been found that VAP increased hospital stay by 10 to 32 days(39). These prolonged hospitalizations underscore the considerable financial burden imposed by the development of VAP.

• Antimicrobial therapy in preceding 90 d
• Current hospitalization of 5 d or more
• High frequency of antibiotic resistance in the community or in the specific hospital unit
• Presence of risk factors for HCAP:
Hospitalization for 2 d or more in the preceding 90 d
Residence in a nursing home or extended care facility
Home infusion therapy (including antibiotics)
Chronic dialysis within 30 d
Home wound care
Family member with multidrug-resistant pathogen
• Immunosuppressive disease and/or therapy

Table 2-Risk factors for multidrug-resistant pathogens causing ventilator associated pneumonia(36)

However, a precise and universal evaluation of such overcosts is difficult. Cost analysis is, indeed, dependent on a wide variety of factors that differ from one country to another, including health care system, organization of the hospital and the ICU, the possibility of patients being treated by private practitioners, cost of antibiotics, and so on(24).

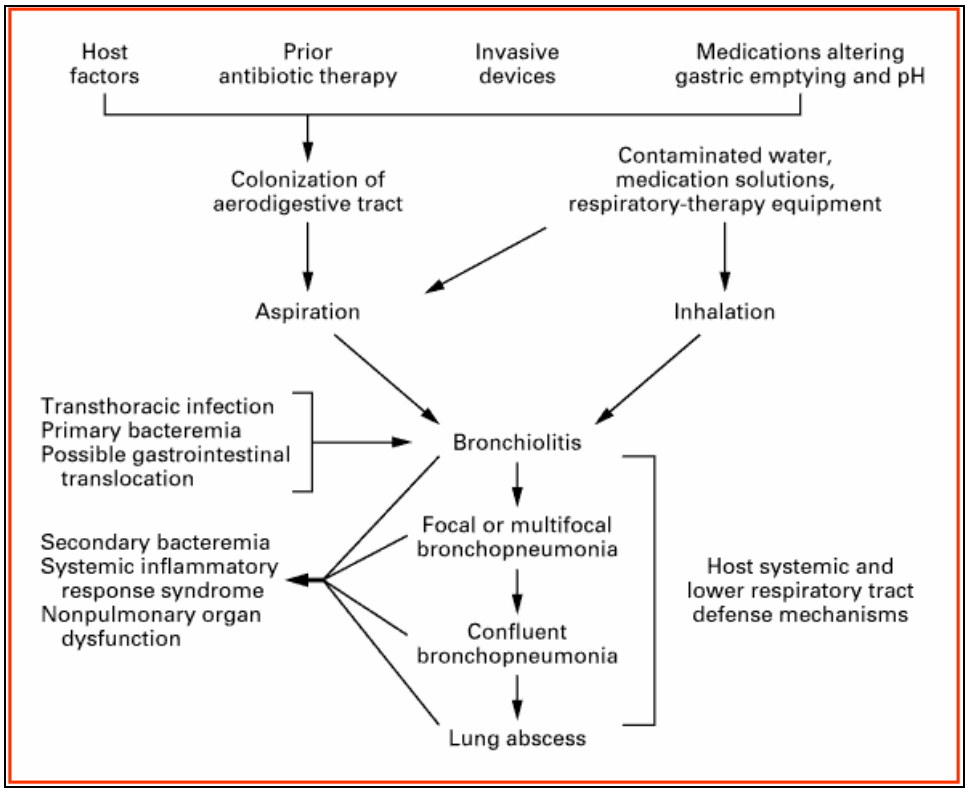

Figure 2-Pathogenesis of Ventilator-Associated Pneumonia(40)

Pathogenesis

The pathogenesis of ventilator-associated pneumonia usually requires that two important processes take place: bacterial colonization of the aerodigestive tract and the aspiration of contaminated secretions into the lower airway. Critical illness leads to the rapid colonisation of the oropharynx with potentially pathogenic bacteria caused by changes in host defences, previous antibiotic exposure, and changes in either the bacterial adhesins or host surface receptors. Any procedure for preventing VAP should be aimed at preventing these two processes(figure 2)(40, 41).

Events important in the progression to pneumonia in intubated patients begin with oropharyngeal colonization by potentially pathogenic bacteria. These events leading to pneumonia are summarized in(Figure 3)(42).

The presence of invasive medical devices is an important contributor to the pathogenesis and development of ventilator-associated pneumonia. Many patients have nasogastric tubes that predispose them to gastric reflux and increase the potential for aspiration(11). The ventilator circuit and respiratory-therapy equipment may also contribute to the pathogenesis of ventilator-associated pneumonia if they become contaminated with bacteria, which usually originate in the patient's secretions(41, 43).

Risk factors

Risk factors provide information about the probability of lung infection developing in individuals and populations. Thus, they may contribute to the elaboration of effective preventive strategies by indicating which patients might be most likely to benefit from prophylaxis against pneumonia(24). Intubation is the most important risk factor

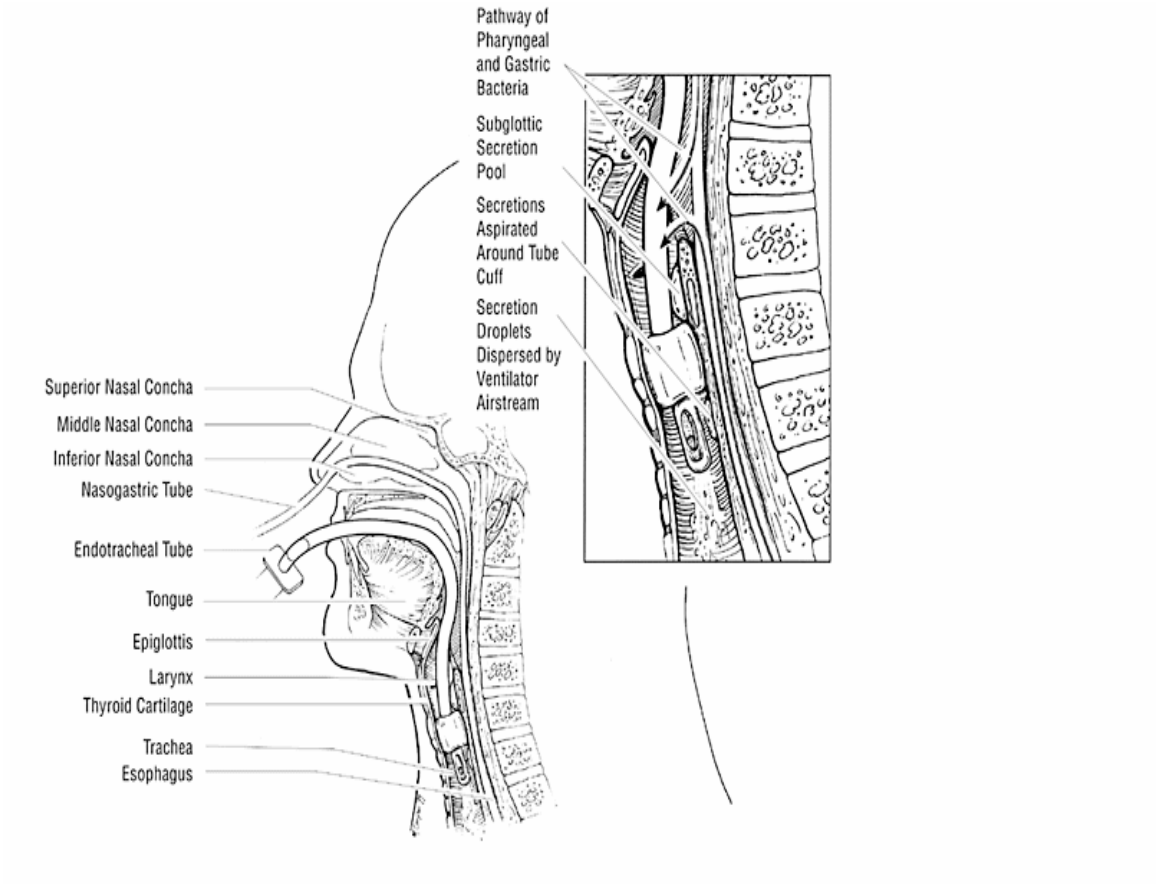

Figure 3- Potential sources of bacteria causing ventilator-associated pneumonia. Bacteria residing in the oropharynx and gastrointestinal tract can contaminate the subglottic secretion pool, as demonstrated. Subglottic secretions above the endotracheal tube cuff are aspirated into the trachea and disseminated into the distal airways and lung parenchyma by the force of the ventilator(42).

for developing nosocomial pneumonia(44).Although it is difficult to differentiate between the risk imposed by the mechanical ventilator and its associated tubing and the presence of a tracheal tube, it is known that the incidence of VAP is less when non-invasive ventilation is used(45).Other major risk factors which have been found to contribute towards VAP is given in Table 3(24).

Diagnosis of VAP.

Various strategies have been developed in the last two decades to diagnose pneumonia in critically ill patients presenting with fever and/or new pulmonary infiltrates on the chest X-ray.These consist mainly of quantitative bacterial cultures of specimen. bronchoscopic and nonbronchoscopic techniques. The accurate diagnosis of VAP still remains problematic. Standard diagnostic features of pneumonia such as fever, tachycardia, leucocytosis, purulent sputum, and consolidation on the chest radiograph are unreliable in the critically ill mechanically ventilated patient(46). Fever, leucocytosis, and tachycardia are non-specific findings and are seen in any critically unwell patient with an inflammatory response to an insult, for example, trauma, burns, pancreatitis, etc. Purulent sputum may be caused by tracheobronchitis and does not always signify parenchymal involvement(47). Infiltrates on the chest radiograph can be caused by a number of non-infective conditions including pulmonary oedema, haemorrhage, and contusions(48).

But more importantly, the use of the “simple” clinical judgement integrating “classical” clinical signs may result in the overtreatment of patients without VAP and in the undertreatment of up to one third of patients with microbiologically proven VAPs(4).However, the use of invasive procedures to diagnose VAP is still a matter of debate among clinicians(49, 50).

INDEPENDENT FACTORS FOR VENTILATOR-ASSOCIATED PNEUMONIA IDENTIFIED BY MULTIVARIATE ANALYSIS IN SELECTED STUDIES*

Host Factors	Intervention Factors	Other Factors
Serum albumin, < 2.2 g/dl	H_2 blockers ± antacids	Season: fall, winter
Age, ⩾ 60 yr	Paralytic agents, continuous intravenous sedation	
ARDS	> 4 units of blood products	
COPD, pulmonary disease	Intracranial pressure monitoring	
Coma or impaired consciousness	MV > 2 d	
Burns, trauma	Positive end-expiratory pressure	
Organ failure	Frequent ventilator circuit changes	
Severity of illness	Reintubation	
Large-volume gastric aspiration	Nasogastric tube	
Gastric colonization and pH	Supine head position	
Upper respiratory tract colonization	Transport out of the ICU	
Sinusitis	Prior antibiotic or no antibiotic therapy†	

Definition of abbreviations: ARDS = acute respiratory distress syndrome; COPD = chronic obstructive pulmonary disease; ICU = intensive care unit; MV = mechanical ventilation.

Table 3-Risk factors for the development of ventilator associated pneumonia(24).

Most authors would agree that the histological examination of lung tissue coupled with the quantitative culture of the tissue may represent an acceptable gold standard, but this is also adequately judged as too invasive in ventilated patients(51).Given the limitations of standard clinical methods and the fact that lung biopsy is often not feasible or definitive in this setting,(52) an easily applicable diagnostic method has been sought.

Clinical criteriae.

The clinical criteriae for diagnosis of VAP was proposed by Johanson etal in 1972. Most researchers have adopted or modified the definition of pneumonia originally used by Johanson et al:'(1) radiographic appearance of a new or progressive pulmonary infiltrate; (2) fever; (3) leukocytosis; and (4) purulent tracheobronchial secretions. The combination of infiltrates on the chest radiograph with two of three clinical criteria had a reasonable diagnostic accuracy(53) In a postmortem study by Fabregas et al., when findings on histologic analysis and cultures of lung samples obtained immediately after death were used as references, a new and persistent (>48-h) infiltrate on chest radiograph plus two or more of the three criteria (i) fever of >38.3°C, (ii) leukocytosis of >12 x 10^9/ml, and/or (iii) purulent tracheobronchial secretions had a sensitivity of 69% and a specificity of 75% for establishing the diagnosis of VAP(54) When all three clinical variables were required for the diagnosis, the sensitivity declined further (23%); the use of a single variable resulted in a decrease in specificity (33%).The clinical criteria yielded a sensitivity of 62% and a specificity of 84% in a study using microbiological criteria for VAP(55). Two necropsy studies have also shown similar results (sensitivity 60% and specificity 80%) when evaluating clinical

criteria(56).As was mentioned earlier individual parameters were found to be very nonspecific for the diagnosis of ventilator associated pneumonia.

Fever

The appearance of a new episode of fever (>38.3 °C) is often the sign for the clinician that the ventilated patient may be developing VAP, and may trigger further diagnostic procedures. But it has been found that as many as 50% of ventilated patients may develop fever for causes that are distinct from pneumonia, particularly in patients with ARDS.(57) It is also noteworthy that VAP can develop without fever, in particular in those patients with continuous veno-venous hemodialysis, receiving NSAIDs or paracetamol, or simply because the sepsis syndrome can be associated with hypothermia(51) Therefore, the introduction of antibiomicrobial therapy for the treatment of VAP suspected on the basis of the sole fever should be avoided, and conversely

the absence of fever should not rule out VAP.

Tracheal aspirates

It has been shown that the increased volume of tracheal aspirates becoming purulent in the last 48 hours was predictive of VAP(58) The routine culture of tracheal aspirates has been understudied as an indication for the development of VAP. In patients intubated for a long period of time, the distinction between colonization and infection is certainly problematic.

Blood leukocytosis

Leukocytosis (>11,000 WBC/mm^3) or leucopenia (<5,000 WBC/mm^3) are frequently used at the bedside as a help to diagnose an infection but is not useful for the diagnosis of VAP.(51)

Radiographic criteria

The development of new pulmonary infiltrates or opacities on the chest X-ray is frequently, with a new fever, the bedside criteria that will trigger the suspicion of a VAP(57). The interpretation of the chest radiogram is often problematic in ventilated patients. This is due to the frequent structural lung abnormalities in ventilated patients (ARDS, COPD), and the possible fluid overload or cardiac failure (lung edema) contributing to the opacities. The diagnosis of VAP based on radiologic criteria suffers from both overinterpretation (false positives) and underinterpretation (false negatives). In the study by Fagon *et al.*, only 31% of the patients with new radiological infiltrates were found to have a microbiologically proven VAP(59) This is corroborated by the study of Meduri *et al*. who found only 42% of the new infiltrates in patients with ARDS could be attributed to an infectious cause(57) .The "best" radiological sign for pneumonia seems to be the presence of an air bronchogram, as demonstrated in a radiological/*post-mortem* examination VAP study(60).Even this sign was associated with a positive predictive value of only 68%.

CPIS score

As indicated above, none of the clinical variables taken separately are predictive enough to be useful at the bedside for the diagnosis of VAP. The association of some clinical variables together seemed to increase the diagnostic yield. With the aim of simulating and quantifying the "clinical judgement", Pugin at al developed in 1991,a score based on 6 variables: fever, leukocytosis, tracheal aspirates,

oxygenation, radiographic infiltrates, and semiquantitative cultures of tracheal aspirates with Gram stain, the clinical pulmonary infection score (CPIS,Annexure 1)(58). The study also found good correlation between clinical score and quantitative bacteriology.CPIS score has been used in various studies mainly for diagnosis and prognostification of the ventilator associated pneumonia and for deciding the duration of antibiotic therapy.The score varies from 0 to 12 points. It was found that a score □6 points was highly predictive of a high burden of bacteria in the lower airways measured by quantitative cultures of the BAL fluid. The advantage of the score over other associations of clinical variables was that it was more flexible and allowed for the signs not to be all present at the same time(58). This greatly increased its sensitivity to diagnose VAP.

The usefulness of the CPIS was confirmed in studies by Flanagan *et al*., and Papazian *et al(61, 62).* These authors found that a threshold of >6 points was associated with sensitivities of 72-85% and specificities of 85-91% to diagnose VAP, a diagnostic yield that matches that of invasive bronchoscopic techniques with quantitative cultures(Table 4).9 In a recent Spanish study, the CPIS, when compared with *post-mortem* histological evidence of pneumonia, had a lower sensitivity and specificity (77 and 42%, respectively) to diagnose VAP(54). The study also used the CPIS with success as a quantitative assessement of the efficacy of oropharyngeal decontamination with topical antibiotics to prevent the development of VAP.(63). The CPIS was further used in an interesting study by Singh *et al(64).* These authors utilized the CPIS (cut-off point >6) as a guide for indicating or withdrawing antibiotic therapy in patients with suspected VAP (= new pulmonary infiltrates). In patients with new infiltrates, but low risk (CPIS

<6), the antibiotic therapy was discontinued if patients remained with a low CPIS after 72 hrs. In patients with high CPIS at the time of admission or at 72 hrs, the antibiotic therapy was continued. This algorithm based on the CPIS was associated with a dramatic reduction in antibiotic use (28 *vs* 97%, p<0.0001) and duration (3 *vs* 10 days, p<0.0001), as well as a marked reduction in overall and antibiotic-related costs(64). Finally, an intriguing report by Fagon *et al* suggests that in patients suspect of having VAP, the noninvasive "clinical" management was associated with a significantly higher mortality (p=0.022) compared to an invasive approach with bronchoscopic sampling of the lower airways and quantitative cultures(65).This study contrasts with others in which such a difference in outcome was not found(66, 67).

Microbiological Diagnosis of VAP

Despite numerous publications on the subject, controversy still exists on the optimal method of microbiological diagnosis of VAP(68). As the trachea and tracheal tube rapidly become colonised with bacteria in the critically ill patient, cultures of sputum or tracheal aspirates may simply yield colonising organisms. The argument therefore revolves around whether specimens of lower respiratory tract secretions should be collected in an invasive manner or whether quantitative analysis of non-invasively collected tracheal aspirates is sufficient. Analysing samples using quantitative culture techniques theoretically permits differentiation between oropharyngeal organisms present at low concentrations and the higher concentrations of pathogenic organisms. Blood cultures have limited value in the diagnosis of VAP and have a very low sensitivity for detecting the pathogenic organism responsible for the pneumonia(69).

Source	Clinical Pulmonary Infection Score	Gold Standard	Sensitivity, %	Specificity, %	LR (95% CI)	
					Positive	Negative
Independent						
Papazian et al,[42] 1995	>6	Histology alone	72	85	4.8 (1.6-14)	0.33 (0.15-0.70)
Fàbregas et al,[45] 1999	>6	Histology and culture	77	42	1.3 (0.75-2.3)	0.55 (0.17-1.8)
Summary					2.1 (0.92-4.8)	0.38 (0.20-0.74)
Nonindependent						
Bregeon et al,[48] 2000	>6	Histology alone	93	85	6.0 (1.7-2.2)	0.08 (0.01-0.56)

Abbreviations: CI, confidence interval; LR, likelihood ratio.

Table 4 : Sensitivity and specificity of CPIS score.

Quantitative cultures of tracheal aspirates

Collection of material for microbiological analysis using this technique is quick, simple, and widely available. While there is some evidence to suggest that the use of this method has a high false positive rate in the diagnosis of VAP, other studies suggest that quantitative analysis of tracheal aspirates offers a reliable alternative to invasive techniques(66, 70, 71). A prospective study by Sanchez-Nieto and colleagues comparing quantitative analysis on non-invasively collected tracheal aspirates with invasively collected respiratory samples in 51 patients with suspected VAP showed a high degree of concordance in bacteriological results and no difference in mortality(66). Another study involving 76 patients with suspected VAP, who were randomly allocated to either invasive or a non-invasive diagnostic strategy, also showed that the invasive strategy had no benefit(67) Both studies used a threshold of 10^5 colony forming units/ml to distinguish tracheal colonisation from true VAP.

A non-invasive strategy of diagnosis in those suspected of VAP seems to be associated with higher antibiotic use(65)

Invasive techniques of sampling distal airways

There are a number of problems associated with the use of bronchoscopy; the expertise and equipment required is not always available and sampling is often followed by a period of hypoxaemia(72).Three comparatively small single centre studies comparing mortality in patients with suspected VAP managed on the results obtained by either invasive studies or quantitative analysis of tracheal aspirates failed to find any difference

in mortality(66, 67, 73). Most recently a meta-analysis of randomised, controlled trials of invasive diagnostic strategies in suspected VAP reported that an invasive approach did not change mortality (odds ratio 0.89, 95% confidence interval 0.56 to 1.41), but did change antibiotic use (odds ratio for change in antibiotic management after invasive sampling, 2.85, 95% confidence interval 1.45 to 5.59)(74).

Currently two techniques are commonly used to obtain distal airway samples with the bronchoscope; BAL or protected specimen brushing (PSB).

The accuracies of tracheobronchial aspirates, protected specimen brush, bronchoalveolar lavage fluid, and protected bronchoalveolar lavage fluid specimens for the presence of pneumonia with microbiologically active pneumonia as the reference test is given in (Table 6)(54). Strategies to be adopted to prevent VAP is given in (Table 5).

Antibiotic treatment of ventilator associated pneumonia

Selection of initial appropriate therapy is an important aspect of care for hospitalized patients with serious infections. Patients at risk for infection with these organisms should initially receive a combination of agents that can provide a broad spectrum of coverage to minimize the potential for inappropriate antibiotic treatment. In the therapy of suspected pseudomonal infection, therapy should involve a selected ß-

Table 5:Selected VAP Prevention Strategies Abstracted From Recent Guidelines

Intervention/Strategy	Support/Evidence	Comments
Infrastructure		
Multidisciplinary team	Programs developed by team consensus are more effective.	Input by critical care staff and respiratory therapists is crucial.
Champion of the cause	Recognized leader/expert increases "buy-in" by staff and hospital administration.	Leadership is needed to set benchmarks, maintain efforts, and secure resources.
Targeted staff education	Staff education/awareness programs have been shown to reduce VAP.	Such programs are adaptable to local needs and are cost-effective.
Infection control	Data support importance in reducing spread of MDR organisms.	Coordinate with quality improvement efforts; feedback data to staff.
Antibiotic control	This reduces inappropriate antibiotic use and associated costs.	Designated pharmacist is optimal; computer programs are good alternative.
Adequate staffing	Critical for maintaining patient safety and adherence to protocols.	This is particularly important in critical care units; current nursing shortages exist.
Benchmarking/quality	Current recommendations from IHI and local multidisciplinary teams.	Benchmarks should be evaluated routinely and data communicated.
Patient care		
Sedation vacation	This is supported by clinical data, and is accessible and feasible.	Implement standard protocols.
Semi-upright position	Supported by early data; recent data suggest lower elevation target indicated.	Few outcome data; poor compliance with strategy. Further studies needed.
NPPV	Supported by several clinical trials in recent review by Cochrane.	Experience with technique is suggested for patients with COPD and congestive heart failure.
Oral care	Evidence is limited, but risk and cost are low.	Further studies are needed.
Stress bleeding prophylaxis	Data support use of PPIs and H_2-blockers; limit to high-risk patients.	PPIs and H_2-blockers are more effective than sucralfate in preventing bleeding.
Deep vein thrombosis prophylaxis	Evidence supportive.	Recommended in the VAP 100,000 Lives Campaign VAP "bundle."
Standardized protocols for weaning and enteral feedings	Rates of VAP are lowered by reduced duration of intubation and enteral feeding.	Protocols help standardize implementation and provide standards for monitoring.
Chlorhexidine with or without colistin	Randomized controlled trials demonstrate efficacy.	More data are needed.
SDD	VAP and mortality decreased with IV plus topical antibiotics.	Concerns about antibiotic resistance limit "routine" use.
Tracheal intubation and use of orogastric tubes	Several small clinical trials report decreased sinusitis.	Recommended but has limited impact on VAP.
Continuous aspiration of subglottal secretions	Decreased VAP shown in at least four RCTs.	Optional; cost and impact on staffing are of concern.
HMEs	Trend toward decreased VAP.	Recommended; eliminates condensate, but decreases humidity.
No change of ventilator circuits	Several RCTs support this intervention.	Recommended; positive cost and staffing impact
Early tracheostomy	Reports from three RCTs; methodologic concerns.	Optional; further data from rigorous studies are needed.
Closed endotracheal suctioning	Three RCTs showed no effect on VAP but probably reduces environmental contamination.	Optional, may reduce environmental spread of MDR pathogens.
Discharge issues		
Vaccination	Pneumococcal and influenza vaccination reduce hospitalizations.	Recommended; poor routine vaccination rates of high-risk populations.
Smoking cessation	Smoking cessation has been demonstrated to reduce morbidity and mortality.	Recommended; instructions and referrals should be documented.
Nutritional counseling	Obesity is a known risk factor for comorbidities associated with pneumonia.	Recommended; instructions and referrals should be documented.
Prevention of aspiration	Aspiration is a major risk factor for pneumonia.	Check sedation, head of the bed; speech and swallow studies, if indicated.

*RCT = randomized controlled trial; HME = heat/moisture exchanger; SDD = selective decontamination of the digestive tract; NPPV = noninvasive positive pressure ventilation; NPPV to table footnotes.

Table 3 Accuracy of non-invasive and invasive diagnostic techniques for ventilator associated pneumonia

Diagnostic technique	*Sensitivity % (n)*	*Specificity % (n)*	*Positive predictive value % (n)*	*Negative predictive value % (n)*
TBA	69 (9/13)	92 (11/12)	90 (9/10)	73 (11/15)
Protected BAL	39 (5/13)	100 (12/12)	100 (5/5)	60 (12/20)
BAL	77 (10/13)	58 (7/12)	67 (10/15)	70 (7/10)
PSB	62 (8/13)	75 (9/12)	73 (8/11)	64 (9/14)
Any invasive diagnostic technique	85 (11/13)	50 (6/12)	65 (11/17)	75 (6/8)
Any non-invasive or invasive diagnostic technique	85 (11/13)	50 (6/12)	65 (11/17)	75 (6/8)

TBA = tracheobronchial aspirates; BAL = bronchoalveolar lavage; PSB = protected specimen brush.

Table 6; Accuracy of non-invasive and invasive diagnostic techniques for ventilator associated pneumonia

Potential Pathogen	Recommended Antibiotic*
Streptococcus pneumoniae†	Ceftriaxone
Haemophilus influenzae	*or*
Methicillin-sensitive *Staphylococcus aureus*	Levofloxacin, moxifloxacin, or ciprofloxacin
Antibiotic-sensitive enteric gram-negative bacilli	*or*
Escherichia coli	Ampicillin/sulbactam
Klebsiella pneumoniae	*or*
Enterobacter species	Ertapenem
Proteus species	
Serratia marcescens	

† The frequency of penicillin-resistant *S. pneumoniae* and multidrug-resistant *S. pneumoniae* is increasing; levofloxacin or moxifloxacin are preferred to ciprofloxacin and the role of other new quinolones, such as gatifloxacin, has not been established.

Table 7:Initial empiric therapy for hospital acquired pneumonia,ventilator associated pneumonia,and health care associated pneumonia in patients with late onset disease or risk factors for multidrug resistant pathogens(54).

lactam plus either an antipseudomonal quinolone or an aminoglycoside. The choice of agents should be based on local patterns of antimicrobial susceptibility, and anticipated side effects, and should also take into account which therapies patients have recently received (within the past 2 weeks), striving not to repeat the same antimicrobial class, if possible.Appropriate antibiotics for the initial management of Ventilator associated pneumonia on the basis of time of onset of disease and risk for MDR pathogens, as outlined in tables 7(54)and and a general guide to antimicrobial therapy is given in table 8(24).

Type of suctioning and ventilator associated pneumonia

While there is no resounding proof that closed suctioning reduces VAP compared to open suctioning, there is also no proof that it increases the risk of VAP. In turn, while observational studies suggest greater colonization of closed-circuit suction catheters, there is no evidence that this increases the risk of VAP. The conventional wisdom that fewer breaks of the circuit result in a lower risk of contamination clearly supports the use of closed-circuit suctioning(75-77). Combes et al randomized 104 patients with negative tracheal aspirates at study entry to open (*n* _ 50) or closed suctioning (*n* _ 54). They found that the incidence of VAP was 3.5 times greater in the open-circuit suctioning group and that VAP increased the length of stay by 17 days(76)..In the recently published metaanalysis,the authors concluded that using closed suction did not provide any benefit on VAP incidence, mortality, or ICU stay of MV patients. Rather suctioning with closed systems was associated with longer MV duration (weighted mean differences: 0.65 days, 95% CI 0.28–1.03) and higher colonization of the respiratory tract (OR=2.88, 95% CI 1.50–5.52) than open suctioning system..

Interestingly, the relevant guidelines seem to be inconclusive on the usefulness of closed TSS in preventing VAP in MV patients. In the most recent guidelines for preventing health-care-associated pneumonia published (2004) by the Centres for Disease Control and Prevention, the preferential use of either the closed TSS or the open TSS for VAP prevention was considered as an unresolved issue(78).In the other hand, the Canadian Critical Care Trials Group and the Canadian Critical Care Society (2004) concluded that type of TSS (closed or open) has no effect on VAP incidence; however, they encouraged the use of closed TSS based on cost considerations(79).A year earlier (2003), the American Association for Respiratory Care's recommendation regarding this issue was that closed TSS should be considered part of a VAP prevention strategy(80). Finally, the European Task Force on VAP (2001) mentioned that there is only limited evidence that closed TSS usage is able to reduce VAP incidence at the expense of a clearly increased cost and, thus, no recommendation has been made(81).

Type of suctioning and effect on environmental contamination.

The conventional method of tracheal toilet requires that the breathing system is opened to atmosphere at the tracheal suction connector to permit the introduction of a sterile suction catheter by a sterile gloved hand. The catheter and the glove are discarded after single patient use in order to minimise bacterial contamination. It is usual for the function of the ventilator to be interrupted during the procedure. An aerosol of droplets of condensate and tracheal secretions can be seen clearly to be expelled from the connector during passive exhalation by the patient and during the positive pressure phase of ventilation by the machine.

CORE ORGANISMS RESPONSIBLE FOR VENTILATOR-ASSOCIATED PNEUMONIA AND RECOMMENDED ANTIMICROBIAL THERAPY

Core Organisms	Core Antibiotics
Early-onset VAP, no specific risk factor	
Enteric gram negative (nonpseudomonal)	Cephalosporin
Enterobacter spp.	Second generation
Escherichia coli	Nonpseudomonal third generation
Klebsiella spp.	or
Proteus spp.	β-Lactam-β-lactamase inhibitor combination
Serratia marcescens	
Haemophilus influenzae	If allergic to penicillin:
MSSA	Fluoroquinolone
	or
Streptococcus pneumoniae	Clindamycin + aztreonam
Late-onset VAP	
Core organisms *plus*	Aminoglycoside or ciprofloxacin *plus* one of the following:
Pseudomonas aeruginosa	Antipseudomonal penicillin
Acinetobacter baumannii	β-Lactam-β-lactamase inhibitor combination
	Ceftazidime or cefoperazone
	Imipenem
	Aztreonam
Consider MRSA	± Vancomycin

Definition of abbreviations: MRSA = methicillin-resistant *S. aureus;* MSSA = methicillin-sensitive *S. aureus*; VAP = ventilator-associated pneumonia. Adapted from the American Thoracic Society (33).

Table 8: Guide to antimicrobial therapy(24).

Ventilators which provide continuous positive airway pressure (CPAP) cause a continuous high flow of gas to be delivered from the open suction connector, and this tends to increase both the quantity and the range of resulting environmental contamination. It is reasonable to suppose that extensive contamination of the environment and the operator occurs directly as a result of the use of this method of tracheal suction(10).

In developing countries where the space allocated to individual beds may be restricted, close proximity of beds may further compound the problem leading to environmental contamination of the respiratory tract. The authors of the recently concluded meta-analysis(12) proposed that studies comparing CES with OES may thus be more relevant in the developing world and may not be paramount issues in countries where occupational health and safety concerns preclude the use of OES and where the ease of use as well as reduced nursing time with CES may over-ride cost concerns. There are studies which looked at the environmental contamination while using the suction catheters.One study showed that the increase in the postsuction colony count detected by the Reuter test when the closed catheter was used (+ **6.7)** was significantly lower ($p < 0.001$) than the increase associated with the open technique **(+25.3).** The organisms were identified **up** to one metre away from the suction site with conventional open suction while closed catheter failed to register any contamination.(Table 9 and Table 10)(10). This finding is consistent with the view that the closed catheter effectively eliminates environmental contamination by organisms from the patient's respiratory tract(10). One study reported that the use of closed-circuit

		Mean difference	SD	*t*-value
Open (conventional)	First day	+30.0	11.8	+7.61 ***
	Second day	+20.7	7.9	+7.82 ***
	Average	+25.3	7.7	+9.88 ***
Closed (Stericath)	First day	+8.1	5.1	+4.78 **
	Second day	+5.2	5.0	+3.19 *
	Average	+6.7	4.0	+5.1 ***
Difference	First day	−21.8	10.4	−6.29 ***
	Second day	−15.3	9.6	−4.79 **
	Average	−18.6	6.6	−8.36 ***

$p < 0.05$ * $p < 0.01$ ** $p < 0.001$ ***

Table 9: Total colony counts measured by air sampling before and after tracheal suction using open or closed suction systems(10).

Distance		Mean difference	SD	*t*-value
50 cm	First day	+13.5	5.4	+7.48 ***
	Second day	+8.6	3.1	+8.43 ***
	Average	+11.0	4.1	+8.14 ***
100 cm	First day	+1.4	1.1	+3.84 **
	Second day	+0.9	1.0	+2.78 *
	Average	+1.2	1.0	+3.54 **

$p < 0.05$ * $p < 0.01$ ** $p < 0.001$ ***

Table 10: Comparison of colony counts on settle plates before and after tracheal suction by the open or closed methods(10).

suction systems results in significantly less environmental contamination, compared to open techniques(10)Though this had no impact on VAP, it does reduce exposure of caregivers.

Type of suctioning and effect on ventilatory parameters.

Multiple studies have been done to look at the hemodynamic parameters while using the open and closed suction catheters.Open suctioning involves disconnection of ventilator from the endotracheal tube.Disconnection itself results in airway pressure drop and loss of lung volume,but a further volume decrease is observed during suctioning(82) due to the generation of negative pressure in the airway.Therefor open suctioning may lead to alveolar collapse and potentially hinders efforts aimed at maintaining lung volume.Hyperoxygenation and hyperinflation maneuvers are often used before and after open suction to limit hypoxemia(17, 83, 84) but do not directly prevent lung collapse.

However closed systems allow non interrupted ventilatory support during suctioning and have been shown to limit or avoid gas exchange impairment and hemodynamic disturbances due to the maneuver(17, 84).A study showed major drop in lung volume during open suction compared to suction with closed suction,SpO2 started to decrease significantly during the open suction and there was an increase in mean arterial pressure during the open suctioning.Increases in mean arterial pressures could result from hypoxemia,airway manipulation and tracheal stimulation(17, 84).Closed suctiong allowed the maintainance of lung volumes,of ventilation and of positive airway pressure during suctioning and avoided decreases in SPo2 and changes in MAP.

Another study conducted in medical and surgical ICU's found that the pO_2 dropped significantly compared to baseline values in the open-system method when PEEP was >8 cm H_2O Five and 15 min after suctioning(85). The maintenance of positive end-expiratory pressure during closed-circuit suctioning has been shown to reduce hypoxemia from lung derecruitment(84, 86).Johnson etal found that open endotracheal suctioning resulted in significant increases in mean arterial pressure throughout the suctioning procedure(17). Both methods resulted in increased mean heart rates. However, 30 secs after the procedure, the open-suction method was associated with a significantly higher mean heart rate than was the closed method. Closed suctioning was associated with significantly fewer dysrhythmias. Arterial oxygen saturation and systemic venous oxygen saturation decreased with open suctioning. In contrast, arterial oxygen saturation and systemic venous oxygen saturation increased with the closed suction method. There was no difference between the two methods in the occurrence of nosocomial pneumonia(17).

A metaanalysis done in 2006 showed that Compared with OTSS(open tracheal suctioning system), endotracheal suctioning with CTSS(closed tracheal suctioning system) significantly reduced changes in heart rate (four studies, 85 patients; weighted mean difference, -6.33; 95% confidence interval, -10.80 to -1.87) and changes in mean arterial pressure (three studies, 59 patients; standardized mean difference, -0.43; 95% confidence interval, -0.87 to 0.00) but increased colonization (two studies, 126 patients; relative risk, 1.51; 95% confidence interval, 1.12-2.04). No conclusions could be drawn with respect to arterial oxygen saturation (five studies, 109 patients), arterial oxygen tension (two studies, 19 patients), and secretion removal (two

studies, 37 patients). Based on the results of this meta-analysis, the authors concluded that there is no evidence to prefer CSS more than OSS(13).

Type of suctioning and cost effectiveness.

One of the main factors influencing the care in ICU especially in developing countries is the cost factor.Unfortunately there are no credible studies looking at the cost effectiveness of the two types of suctioning from the developing countries.In a randomized, controlled study by Lorente etal, VAP incidence and costs of suctioning were assessed in 457 mechanically ventilated patients assigned to the open-suctioning technique or to a closed system which allows partial (suctioning catheter with its protected covering sheath) or complete system change. The closed system was changed not routinely but only when it presented mechanical failure or visible soil (partial change), or when the patient needed reintubation (complete change). No difference was found between groups in the rate and incidence density of VAP or in the distribution of micro-organisms responsible for VAP. Costs of suctioning were similar between open and closed

suctioning, but they varied according to the length of mechanical ventilation: costs associated with use of the closed system were higher than those with open-suctioning when mechanical ventilation was shorter than 4 days and lower when the length of mechanical ventilation was greater than 4 days.They also found that , the aspiration cost was less expensive in the CTSS without periodic change group than in the OTSS group ($1.89 × 1.53 vs $2.45 × 0.71 per patient-day, $P < 0.0001$).They also concluded that

Study	Costs CTSS	Costs OTSS	Comments
Adams 1997	Average daily costs: £16.89 sterling	Average daily costs: £1.45 sterling	
Johnson 1994	Daily cost: US$13.00	Daily cost: US$14.88	Results based on a unit average of 16 suctioning procedures per patient per day
Lorente 2005	Patient costs per day: US$ 11.11±2.25	Patient costs per day: US$ 2.50±1.12	
Lorente 2006	Patient costs per day: eur 2.3±3.7	Patient costs per day: eur 2.4±0.5	For patients ventilated lower than 4 days the CTSS costs were higher than those of the OTSS (CTSS = eur 7.2±4.7 vs OTSS = eur 1.9±0.6; P<0.001). This trend changed for the patients ventilated longer than 4 days (CTSS = eur 1.6±2.8 vs OTSS = eur 2.5±0.5; P< 0.001)
Zielmann 1992	Patient costs per day: eur 27.35	Patient costs per day: eur 9	Results based on an average of 15 suction procedures

Table 11:Costs:comparing open and closed suction systems(87).

CTSS without periodic change decreased the aspiration cost and did not modify the VAP incidence(21).

Because in-line suction catheters are parts of the ventilator circuits, they should be changed for each new patient and as clinically indicated and not at regular intervals for infection control purposes(79). Such a policy is highly cost-effective and could decrease the risks of patient cross-contamination and healthcare provider exposure to respiratory secretions during changes of the closed system(79). The maximum safe duration of closed-suction systems in use on a single patient, however, remains unknown(88).Another study done by Johnson etal found that Open endotracheal suctioning cost $1.88 more per patient per day and required more nursing time compared to closed suction without any difference in VAP rates(17).Most of the other studies have shown that costs were much higher for the closed suction.(Table 11)(87).

Type of suctioning and nursing related outcomes.

OS is performed by disconnecting the patient from the ventilator and introducing a suctioning catheter into the endotracheal tube(ETT). Nursing personnel using sterile gloves are necessary for this procedure. One person opens the connection between the ETT and the ventilatory tubing system; the second person introduces a suctioning catheter and performs flushes. Usually, two to three suctioning catheters are necessary to complete suctioning. Different catheters are used for suctioning the trachea and the oropharynx.While closed suction catheter is attached between the ETT and the ventilatory tubing system. This system, included in the ventilatory circuit, allows introduction of suctioning catheters into the patient's airway without the necessity of

disconnecting the patient from the ventilator(89). But suctioning of the oropharynx with a open suction catheter is needed while using closed catheter for the endotracheal tube.

Results from Zielmann 1992(90) and Johnson 1994(17) reported that nurses needed more time to suction patients with OTSS. Zielmann 1992 observed that nurses averaged 3.5 minutes (range of 2 to 6 minutes) to suction patients with OTSS, whereas suctioning patients with CTSS(closed tracheal suctioning system) took one minute less (average = 2.5 minutes, range 2 to 4minutes). Johnson 1994 reported overall shorter times than those of Zielmann 1992 but the differences between groups remained. These authors reported an average of 2.5 minutes for the OTSS in comparison with the 1.5 minutes needed to suction with the CTSS(91).

META ANALYSIS OF TRIALS DONE ON CLOSED AND OPEN ENDOTRACHEAL SUCTIONING SYSTEM.

There have been multiple metaanalysis done regarding the usefulness of closed endotracheal suctioning system over open endotracheal suction.None of the Metaanalysis found any benefit in using CTSS over OTSS.

Metaanalysis done by Siempos etal(92) which looked at 9 Randomized control trials and found no difference in the incidence of VAP between patients managed with closed and open TSS [odds ratio (OR)=0.96, 95% confidence intervals (CI) 0.72-1.28]. There was no heterogeneity among the eligible trials (I^2=0, 95% CI 0-0.65). The compared groups did not differ with respect to mortality (OR=1.04, 95% CI 0.78-1.39) or intensive care unit (ICU) length of stay [two RCTs: 12.3 (SD 1.1) *vs* 11.5 (1.4) days and 15.6 (13.4) *vs* 19.9 (16.7) days]. However suctioning with closed systems was associated with longer MV duration (weighted mean differences: 0.65 days,

95% CI 0.28-1.03) and higher colonization of the respiratory tract (OR=2.88, 95% CI 1.50-5.52) than open TSS.

Another metaanalysis done by Jongerden etal(13) also did not find any difference between the two suctioning systems with regard to ventilator-associated pneumonia and mortality.But they found that compared with OSS, endotracheal suctioning with CSS significantly reduced changes in heart rate (four studies, 85 patients; weighted mean difference, -6.33; 95% confidence interval, -10.80 to -1.87) and changes in mean arterial pressure (three studies, 59 patients; standardized mean difference, -0.43; 95% confidence interval, -0.87 to 0.00) but increased colonization (two studies, 126 patients; relative risk, 1.51; 95% confidence interval, 1.12–2.04).They also found CSS to be more expensive than OSS.

Another metaanalysis done in our institution(Peter etal)(12) also didnot demonstrate a superiority of CES over OES with respect to VAP or mortality. However they went on to say that in developing countries where the space allocated to individual beds may be restricted,close proximity of beds may lead to environmental contamination of the respiratory tract. The high incidence of pulmonary tuberculosis in developing countries poses greater risk to the health personnel, and the mode of suctioning assumes greater importance. Thus opined that studies comparing CES with OES may be more relevant in the developing world and may not be paramount in countries where occupational health and safety concerns preclude the use of OES and where the ease of use as well as reduced nursing time with CES may override cost concerns.They also stressed about the increased need for trials from the developing countries which was the basis for doing this trial.

METHODOLOGY

This trial was a ***Randomized controlled equivalence trial (RCT)*** comparing closed endotracheal versus open endotracheal suctioning in mechanically ventilated medical intensive care unit patients. Randomization was performed using varying block sizes and was computer generated. Programme allocation was concealed with the use of sealed envelopes.

It was a prospective study which looked at all the patients admitted to ICU on ventilator. Patients were enrolled after informed consent. They were randomized into either the open or closed suction arm. Data collection:

After the patient is recruited to the trial, all relevant data were collected in DATA Abstraction forms(ANNEXURE II)that included the following (copy of data abstraction form enclosed).

*Indication for admission

*Past medical history

*Vital signs

*Arterial blood gas

*Oxygen saturation using a pulse oximeter

*Chest Radiograph

*Ventilator settings at admission

*In patients who fulfill the criteria of Ventilator associated pneumonia, suction tip culture and sensitivity and Blood culture and sensitivity

*Data regarding anti-microbial therapy

*APACHE ll score(ANNEXURE III)

Data was collected till the duration of hospitalization in ICU, death or discharge from ICU.

The results were compared and analyzed statistically to see if there are significant differences between the usage of closed endotracheal suctioning compared to open endotracheal suctioning in terms of the parameters studied.

The results were analyzed using SPSS version 15. Data was analysed statistically initially comparing each variable by internal cohort while looking at the outcome**. Chi square test** was the test of significance in this study. Mann-whitney U test was used for the comparison of medians. . Odds ratio (OR) and confidence intervals (CI) were calculated and a 'p' value less than 0.05 was considered statistically significant. All reported p values are two-sided. Univariate analysis and multivariate analysis were performed to assess the risk factors for clinical outcome among he study patients.

The study design and methods were approved by the Fluid Research Committee, Christian Medical College, Vellore.The study was funded by Fluid Research Committee, Christian Medical College, Vellore and Tyko Health care who sponsored the closed suction catheters.They did not have any role in the design,conduct,manuscript writing of any part of the study.

Participants

Adult patients (aged 18 years or over) admitted to the medical ICU requiring invasive mechanical ventilation at admission or within 24 hours of admission to the ICU were enrolled to the study.

Intervention

All patients who are invasively mechanically ventilated require toileting of the respiratory tract for the purpose of clearing respiratory secretions. This was normally performed in our ICU after disconnection of the respiratory circuit and employing a single-use-suctioning catheter under aseptic precautions. Given the clinical equipoise comparing open versus the more recently described closed method of endotracheal suctioning; patients was randomized to have either open or closed endotracheal suctioning. Closed endotracheal suctioning was performed without disconnection from the respiratory circuit employing multi-use in-line-suctioning catheters.

Inclusion Criteria:

1) All adult patients (> 18 years) presenting to Medical ICU.
2) Patients on mechanical ventlation at admission or requiring invasive mechanical ventilation within 24 hours of admission to medical icu .
3) Willingness to participate in the trial

Exclusion Criteria:

1) Patients not requiring invasive mechanical ventilation
2) Patients unwilling to participate
3) High respiratory supports where the clinician deems that patients should have closed endotracheal suctioning
4) Post cardiac arrest

Withdrawal criteria:

1) Patient unwilling to continue participation in the trial.

Outcome measures

The following outcome parameters were specifically assessed in this study. These outcomes are defined as follows:

.

1. ***Ventilator associated pneumonia*** *was considered if the following criteria are observed(25).*

   New and persistent radiographic infiltrate plus 2 of the following:

   - Body temperature > 38º Celsius or < 36º Celsius without obvious extra pulmonary infectious source,
   - White blood cells >10, 000 or < 4000.
   - Macroscopically purulent tracheal aspirate

A postmortem study had established 69% sensitivity and 75% specificity for the above diagnostic rule(54).

The CPIS score was used along with the above criteria to corroborate the diagnosis of VAP.

Early VAP-VAP developing <4 days.

Late VAP-VAP developing >4 days.

2. ***Mortality:*** defined as deceased when discharged from hospital or ICU.
3. ***Left basal collapse:*** as per the radiological findings that would be reported by a radiologist blinded to the study.
4. ***Cost:*** included costs of suctioning (catheter cost, gloves) and not for the full hospital admission.
5. ***Arterial desaturation:*** defined as the saturation drop of > 5% and/or < 90% or more as picked up by the saturation probe of the pulse oximeter.

SAMPLE SIZE CALCULATION:

Though incidence of VAP can range from 6.8% to 44% as shown by various studies, a meta analysis done in our institution showed an overall incidence of 18.63% in open suctioning group and 19.75% in the closed suctioning group(personal correspondence,5). An equivalence study with 80 percent power and 5% alpha error was planned so that a difference of upto 14 % would be cosidered as an equivalent difference between the two groups ie:there is no difference between the two groups.

Hence the sample size taken into each arm was 100.

RESULTS

Population characteristics:

A total of 693 were admitted to the medical ICU (MICU) during the time period of June 1st 2007 to Feb 14th 2008.Out of 693 patients 448 were intubated and ventilated. 248 patients were excluded (the reasons for which are given in figure 4) and 200 patients were randomized into closed (N=100) and open (N=100) suction arms.

The baseline characteristics are shown in Table12A and 12B.Both groups had similar population charecteristics except for ischaemic heart disease which were more common in the open group(P = 0.018).The mean APACHE score for open group was 21.05(SD-6.16) and for closed group was 20.82(SD-6.33)which was not statistically different.

There was equal male and female representation. Non Invasive ventilation was used in 6% and 4% of patients in the closed and open group prior to invasive mechanical ventilation. Most patient underwent emergency intubation and most were admitted from the emergency department.

Figure 4:Patient flow chart.

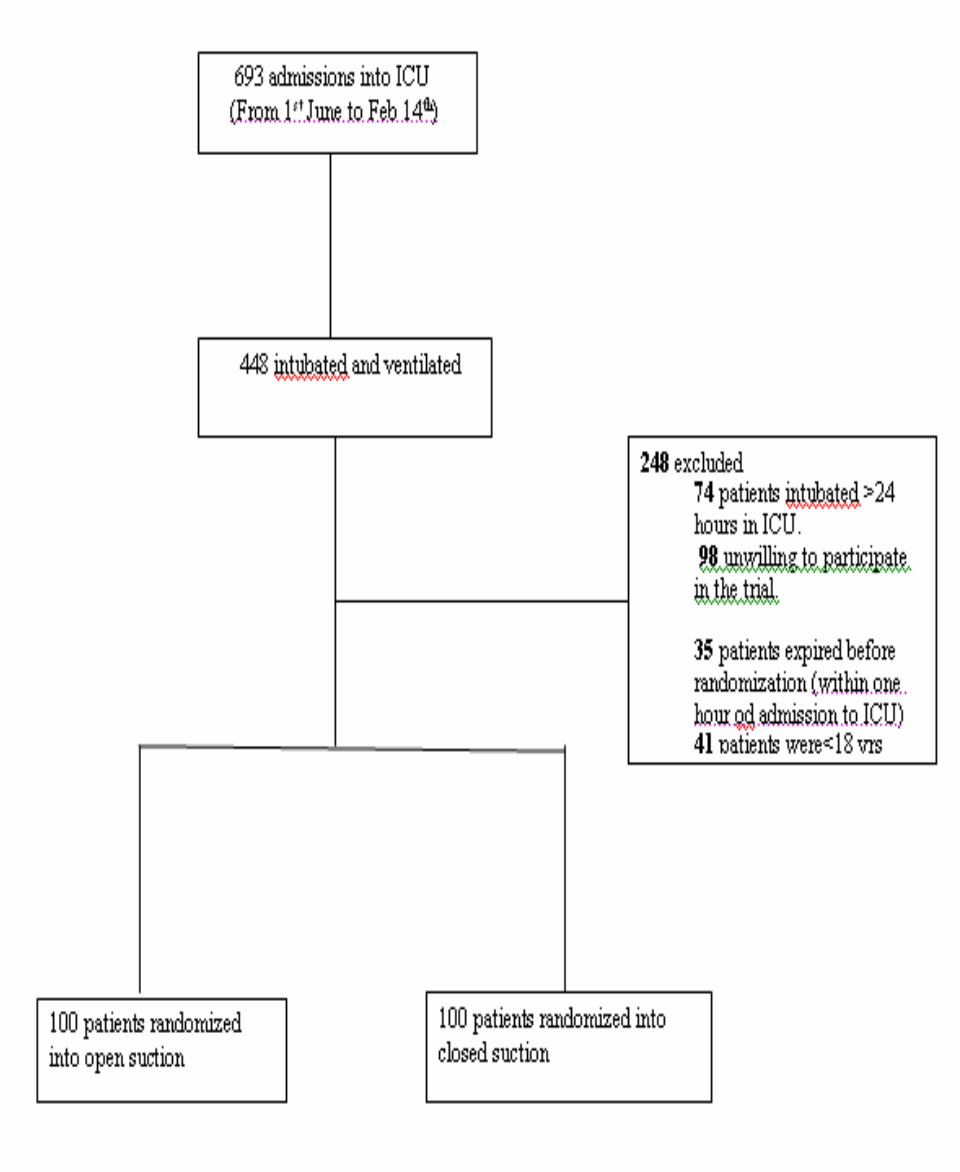

Table12 A:Baseline charecteristics-Demographic Data and Comorbidities.

BASELINE CHARACTERISTICS	OPEN SUCTION (n=100)	CLOSED SUCTION (n=100)
Demographic data		
Age(mean)	44.01 (16.2)	41.68 (15.9)
Male Female	50 50	54 46
Co morbidities		
Diabetes	16	20
Hypertension	17	16
Dyslipidemia	4	1
Ischaemic Heart Disease	1	9
Peripheral Vascular Disease	1	0
Cerebro Vascular Accident	2	1
Chronic Obstructive Lung Disease	3	5
Smoking	4	4
Malignancy	11	12
Chronic Liver Disease	0	1
Chronic Renal Failure	9	7
HIV Status	3	0
Other Respiratory Diseases	7	6

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Table 12B:Baseline characteristics-Prior NIV use, Previous medications, Reason for admission and Type of intubation.

Prior NIV use Prior NIV used	6	4
Reason for admission Respiratory failure Hemodynamic support Neurologic Respiratory Failure and Hemodynamic support	 40 15 2 43	 46 13 5 36
Previous medications Steroids Aspirin Statins HAART Immunosuppresives Others None	 5 6 1 3 11 1 73	 5 5 1 0 13 9 67
Type of Intubation Emergency Elective	 83 17	 78 22
Place Of Intubation ICU Emergency Department Wards Previous Hospital	 14 49 35 2	 5 51 40 4

The most common co-morbidities were diabetes(18%) and hypertension(16.5).The number of ischaemic heart disease patients were more in the closed group(9%) than open group(1%) with a p value of 0.018.Most of the patients were from general medicine(71.5%).The reasons for majority of admissions to medical ICU were respiratory failure and haemodynamic instability.

30% patients were already on medications prior to admission to medical ICU.The medications included steroids,aspirin,statins,antiretroviral medications,immunosuppresives and others(antiparkinsonism drugs,oral hypoglycaemic agents).There were no differences in the medications between the two groups(p value-0.128).

Patients who were started on noninvasive ventilation(NIV) prior to intubation were similar in both groups.6% in open group and 3% in closed group with a P valve of 0.364.The mean duration of NIV was less than one day in both groups.The place of intubation was similar in both groups(p value-0.151) with 17% in the open and 22% in closed group were electively intubated (p value 0.372).

OUTCOME MEASURES.

1)Ventilator associated pneumonia and method of suction.

The incidence of ventilator associated pneumonia was calculated according to the clinical criteria and was confirmed with more stringent criteria by taking into account CPIS score also. Total incidence of VAP was 23.5% according to clinical criteria and 14% according to clinical criteria with CPIS score. According to clinical criteria the incidence of VAP was 29% in open group and 18% in closed group with a p value of 0.067(95% CI 0.91-3.83)(Table 13).When both clinical criteria and CPIS score was taken for the diagnosis of VAP,the incidence was 18% in open and 10% in closed group with a p value of .103(95% CI 0.81-4.91).

Table 13: Incidence of ventilator associated pneumonia and Type of suctioning

Method of diagnosis of VAP	Method of Suction		P value	Total
	OPEN SUCTION (N=100)	CLOSED SUCTION (N=100)		
Clinical Criteriae	29	18	0.067	47
Clinical criteriae and CPIS score	18	10	0.103	28

The number needed to treat to prevent one VAP was 9 patients with closed suction catheter,taking into consideration only clinical criteria.When more

stringent criteria of clinical criteria with CPIS score was taken the number needed to treat was 12.5 patients.

2) Early Vs Late VAP

VAP was classified into early and late depending on the day of development of ventilator associated pneumonia.Of all the people who developed VAP 44.68 % had a early VAP(Table 14).Out of 29 people who developed VAP in the open group 11 patients had early VAP(37.93%). While in the closed group out of 18 patients who developed VAP,10 patients developed early VAP(56%).The incidence of Early VAP was similar in both groups(P value 0.81) while Late VAP was significantly more in open group(P value 0.03) than the closed group.

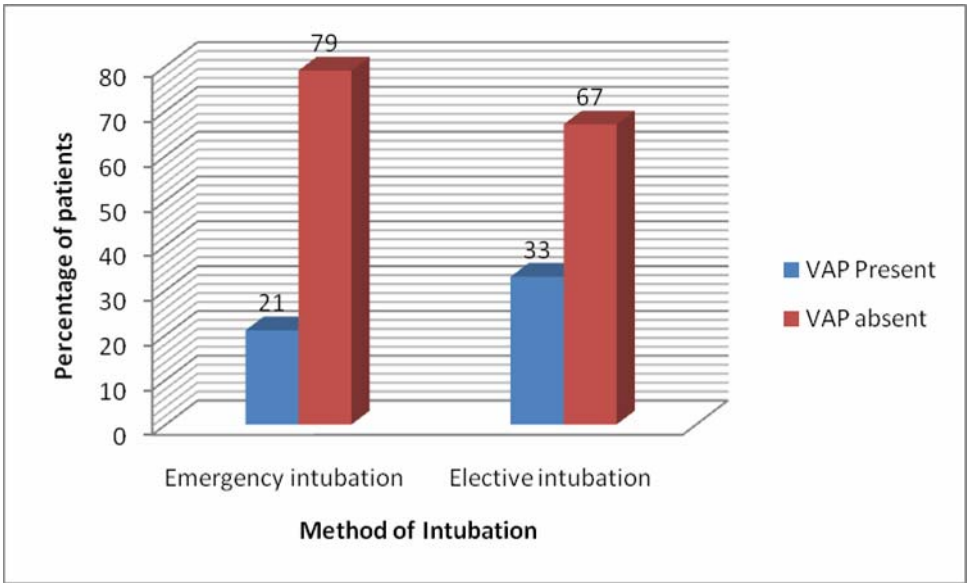
Table 14:Method of suction and Timing of VAP.

Timing of VAP	OPEN SUCTION	CLOSED SUCTION	P Value	Total
EARLY VAP	11	10	0.81	21
LATE VAP	18	8	0.03	26
Total	29	18		47

3) Emergency Vs Elective intubation

21% of those who required emergency intubation developed VAP while 33.33% of those who was electively intubated developed VAP with a P value of 0.106(Figure 5).

Figure 5:Method of intubation and VAP(%)

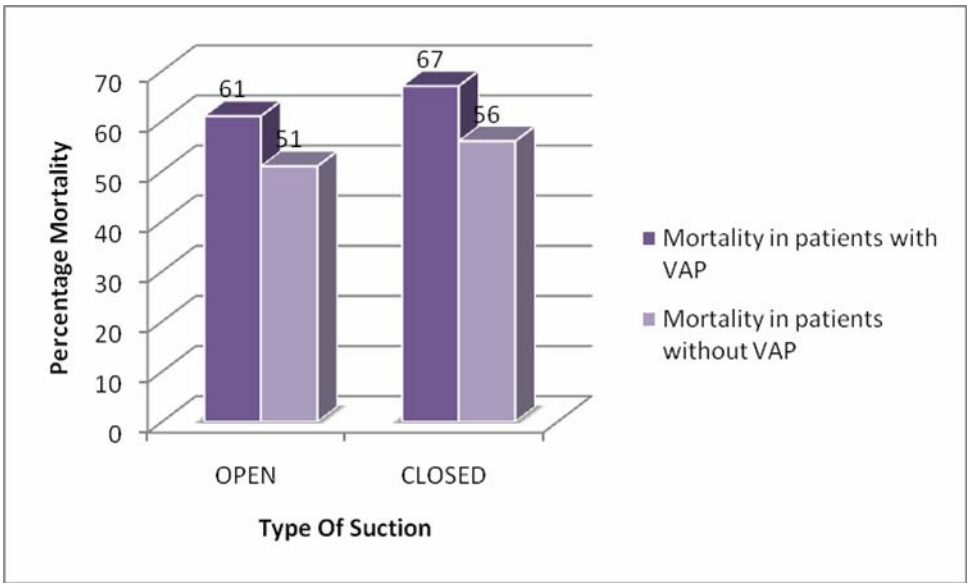


(P value = 0.106)

4) Mortality in VAP

There were no difference in mortality between the patients who developed VAP in both open and closed groups(Figure 6). Patients who developed VAP had a mortality of 40.42%.). There was no difference in the timing of VAP and Mortality;P value 0.06(figure 7).

Figure 6: Mortality in patients with VAP.



(P value = 0.99)

5) Microbiology Of VAP

Of the 47 people who was diagnosed with VAP,endotracheal suction from 5 did not grow any organisms,10 patients had monomicrobial infection and rest had polymicrobial growth.The most common organism isolated was Pseudomonas(63.8) followed by Non fermenting gram negative organisms other than Pseudomonas(NFGNB) (36%) and Klebsiella(32%)(Figure 8).There were no difference between the two groups in the number of organisms isolated(Table 15 and Figure 9).

Figure 8: Percentage of patients with each organism.

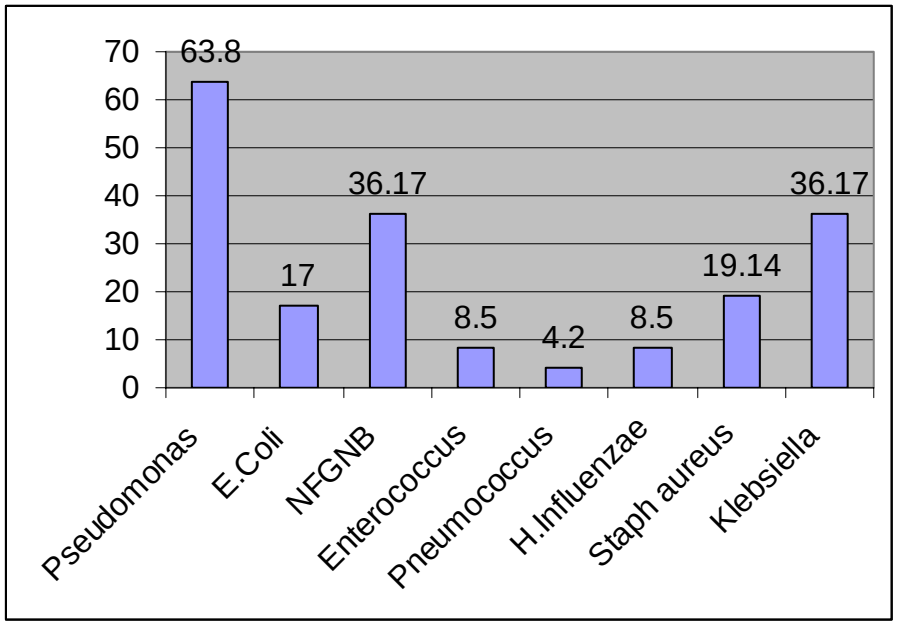


Figure 9: Percentage of each organism in patients who developed VAP in Open and Closedsuctiongroups.

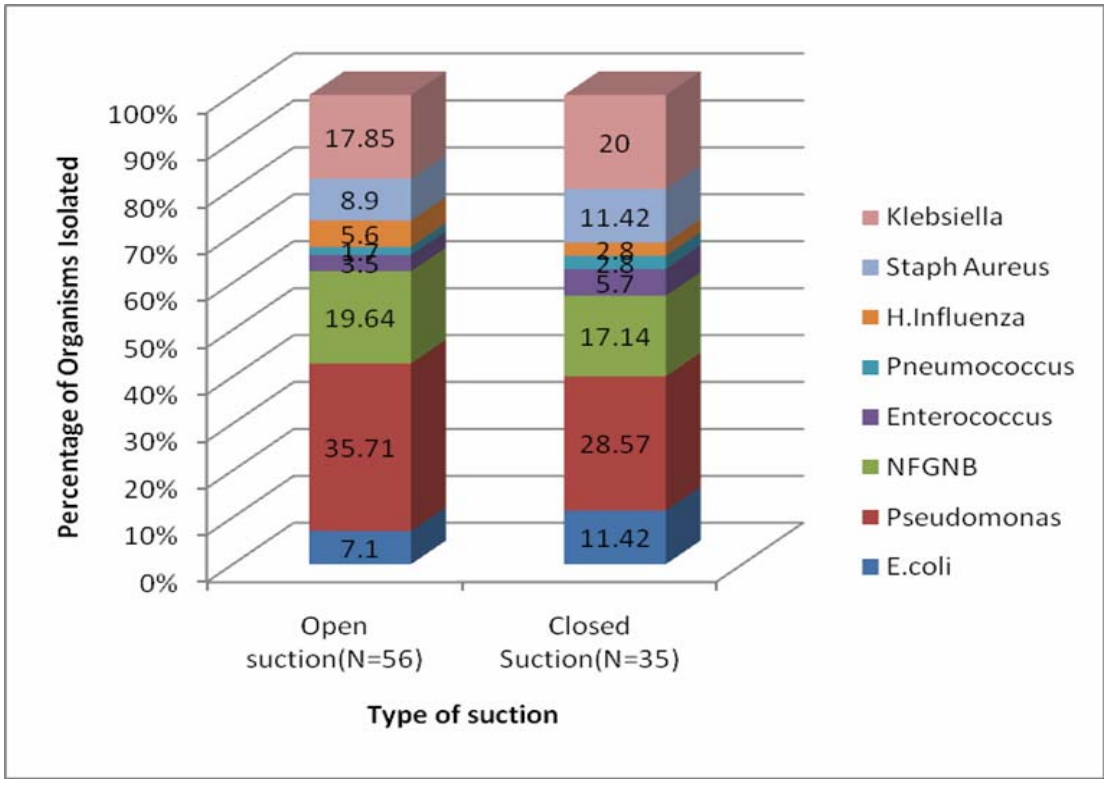
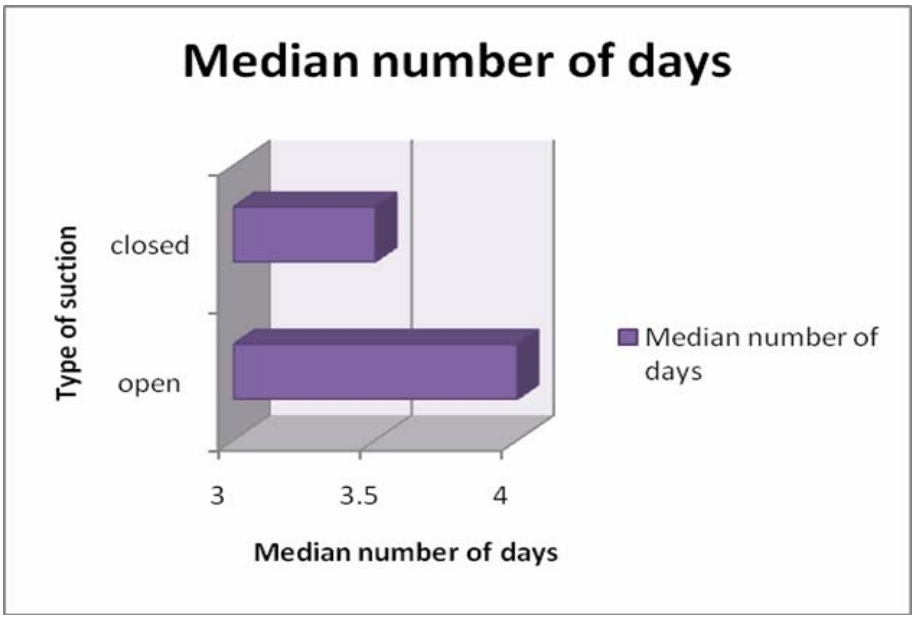


Table 15 :Number(percentage) of Organisms isolated in each group in patients with VAP.

Organism	Open suction(n=56)	Closed Suction(35)	P Value
E.coli	4(7.1%)	4(11.42)	0.22
Pseudomonas	20(35.71)	10(28.57)	0.36
NFGNB	11(19.64)	6(17.14)	0.71
Enterococcus	2(3.5)	2(5.7)	0.571
Pneumococcus	1(1.7)	1(2.8)	0.651
H.Influenza	3(5.6)	1(2.8)	0.30
Staph Aureus	5(8.9)	4(11.42)	0.49
Klebsiella	10(17.85)	7(20)	0.72

Figure 10:Median days to VAP and type of suction.



(P value -0.218)

The median no of days for development of ventilator associated pneumonia after the mechanical ventillation was 4 days in open and 3.5 days in closed(Figure 10).

Mortality and method of suction

The total ICU mortality(Table 16) was 44.5% and hospital mortality was 52.5%.Comparing the Hospital mortality(Table 17),Open group had 57% hospital mortality rate while Closed group had 48% with a P value of 0.203 which was not significant. ICU mortality was 47% in the open group and 42% in the closed groupwith a P value of 0.477.

Table 16:Status at discharge from ICU and Type of suction.(P value 0.477)

	TYPE OF SUCTION			
STATUS AT DISCHARGE FROM ICU	OPEN	CLOSED	TOTAL	P VALUE
ALIVE	53	58	111	0.477
DIED	47	42	89	
TOTAL	100	100		

Table 17:Status at discharge from Hospital and Type of suction(P value 0.203).

	TYPE OF SUCTION			
STATUS AT DISCHARGE FROM HOSPITAL	OPEN	CLOSED	TOTAL	P VALUE
ALIVE	43	52	100	0.203
DEAD	57	48	100	
TOTAL	95	105		

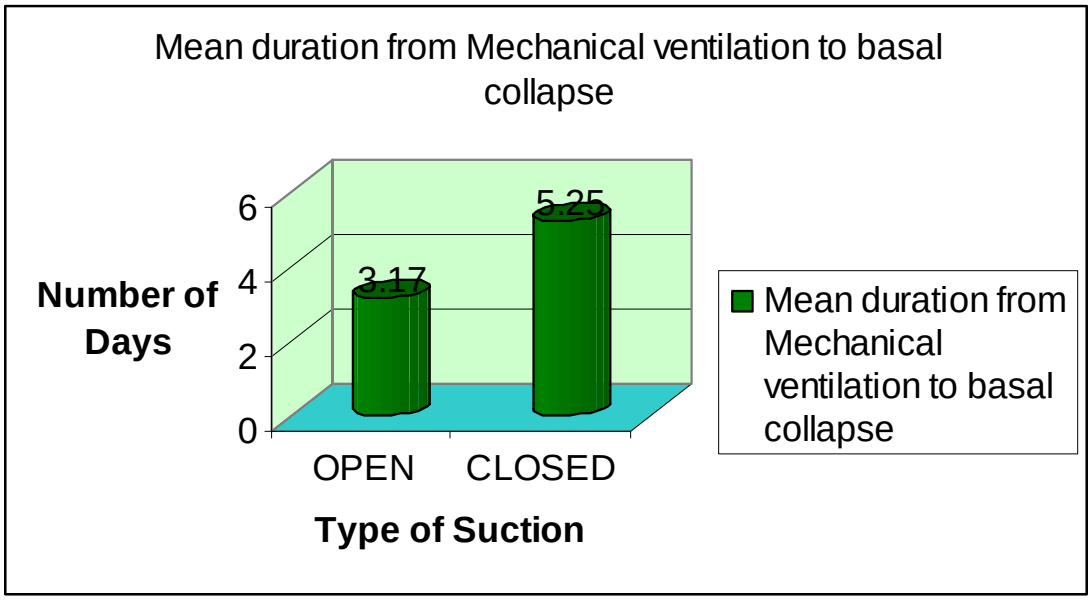
Basal collapse and method of suction.

Comparing the open and closed groups,the left basal collapse was more common in the open group(14%) than in the closed group(5%) with a P value of 0.03 which was statistically significant(Table 18).The mean duration for development of basal collapse was 3.17 days in open group(SD-2.4) and 5.25 days in closed group(1.893)(figure 11).9% in the closed group and 4% in the open group developed pneumothorax but there was no statisticaly significant difference between the two groups.

Table 18 :Method of suction and left basal collapse(P value 0.03)

	OPEN SUCTION	CLOSED SUCTION	P VALUE
PRESENCE OF BASAL COLLAPSE	14%	5%	0.03

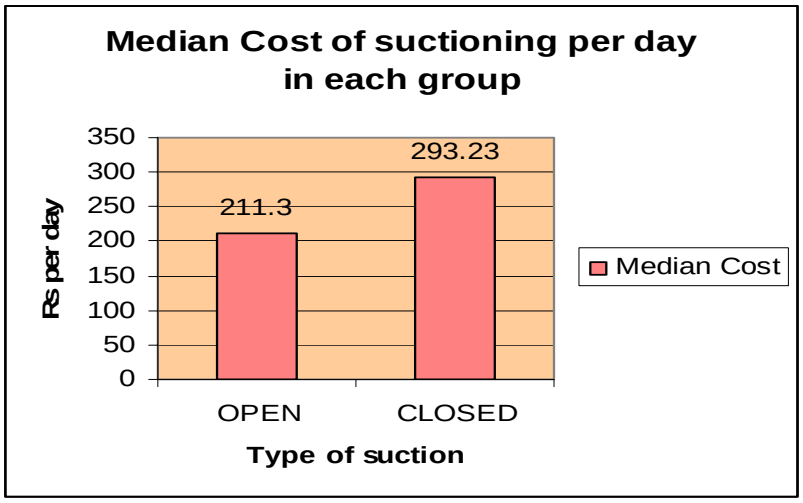
Figure 11:Mean duration(days) to development of basal collapse and method of suction.



Method of suction and cost related issues.

Costs were compared between closed and open suctioning systems.Suctiong costs included the amount spend for the gloves as well as the suction catheters.The median cost of suctiong per day by using closed suction was 293.23 Rs(IQ range-92,602) and by using open suction was 211.30 Rs(IQ range 152,560)(Figure 12).Comparison between the two medians by using the Mann Whitneys test did not yield ant significant difference with P value of 0.2.

Figure 12: Cost of suction per day in closed and open suction groups.



(P value 0.2)

DURATION OF VENTILATION,ICU AND HOSPITAL STAY

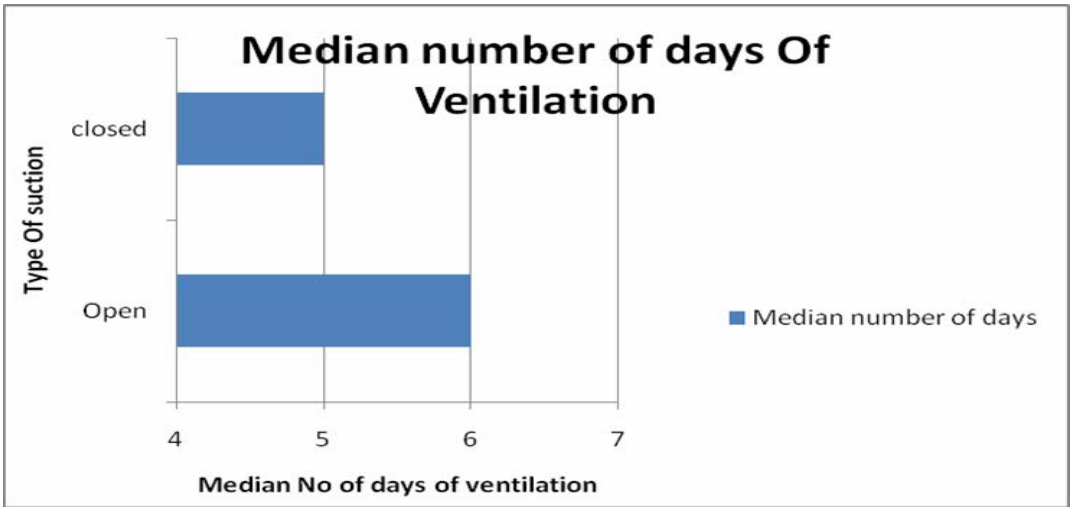
Mean duration of ventilation was 6 days in open group and 5 days in the closed group(p value -0.651)(Figure 13).The mean duration of stay in ICU was 8.01 days in the open group(95% CI**:**6.58-9.44) and 7.34 days in the closed group(95% CI**:**6.18-8.5).The hospital mean duration of stay was 14.04 days in the open group(95% CI-11.52-16.56) and 16.42 days in the closed group(95% CI-13.11-19.73).

Method of suction and Haemodynamic parameters.

The median duration of suction in both groups were 6 minutes.The difference in oxygen saturation was 1.96 and 1.63 in open and closed groups(Table 19).Mean heart rate increased by 1.58 in open while only .06 in the closed group.Mean arterial pressure went up by 0.78 in open and 0.28 in the open group.

The outcome measures have been outlined in the (Table 20A and 20 B) .

Figure 13: Mean duration(days)of Ventilation in ICU and the type of suction.



(P Value:0.651)

Table 19:Haemodynamic parameters and the type of suction.

HEMODYNAMIC PARAMETERS (MEAN DIFFERENCE BEFORE AND AFTER SUCTION)	OPEN SUCTION	CLOSED SUCTION
OXYGEN SATURATION	+1.96	+1.63
HEART RATE	+1.58	+0.06
ARTERIAL BLOOD PRESSURE	+0.78	+0.28

Table 20A:Outcome Measures

Outcome measures	**open**	**closed**	**Odds ratio**	**95% confidence intervel**
Ventilator associated pneumonia Clinical criteriae	29(14.5%)	18(9%)	1.86	(0.91 to 3.83)
Ventilator associated pneumonia Clinical criteriae with CPIS score	18(9%)	10(5%)	1.98	(0.81 to 4.91)
Timing of VAP-Early VAP Clinical criteria Clinical criteria +CPIS score	 11(52%) 6(66%)	 10(48%) 7(54%)	 1.17 1.49	 0.65-2.12 0.87-2.57
Timing of VAP-Late VAP Clinical criteria Clinical criteria +CPIS score	 18(69%) 12(80%)	 8(31%) 3(20%)	 4.95 16	 2.61-9.46 7.6-34.18
Mortality rates ICU	47(47%)	42(52%)	1.22	(0.67 to 2.23)
Mortality rates Hospital	57(57%)	48(48%)	1.44	(0.79 to 2.61)
Left basal collapse	14(14%)	5(5%)	3.09	(0.99 to 10.31)

Table 20 B :Outcome measures

Outcome measures	**Open**	**Closed**	**Pvalue**
Median cost of suction per day	211/-(IQ range 152,560)	293/- (IQ range-92,602)	0.20
Median (Range) duration of ICU stay(days)	6.0 (1-35)	6.0(1-26)	0.99
Median (Range)duration of Hospital stay(days)	12 (1-80)	11.5 (1-98)	0.48
Median(Range) Duration Of ventilated days	6(1-39)	5(1-29)	0.651

* Mann-whitney U test for the comparison of medians

DISCUSSION.

Though multiple randomized control trials have been done on the advantages and cost effectiveness of the closed suction catheter system over open suctioning system,there haven't been any studies about the same done in developing countries. This study from a developing country looks at the cost effectiveness of the two suctioning systems and its advantages in preventing ventilator associated pneumonia and reducing the mortality and the duration of hospital stay.

The postulated advantages of closed endotracheal suctioning system have not been shown to translate into clinically meaningful improvements(11). Most of the studies done in developed countries did not show any advantage of closed suctioning over open suction except in maintaining the hemodynamic parameters during the suction. Several metaanalyses have been done on this issue, but none of them found closed suctioning to be advantageous over open suctioning system.

This study was done in the 11 bedded medical ICU of a tertiary care hospital in India during the period from June 1st 2007 to Feb 15th 2008.652 patients were admitted into the medical ICU during this time period of which 448 were intubated. 200 patients were finally included into the study of which 100 each were randomized into open and closed suctioning systems.The baseline characteristics were similar in both groups except for co-morbidities in which ischaemic heart disease patients were more in closed group than in open group.However it is unlikely that this variable has affected the outcome of the study(VAP).

6% of patients in open group and 4% in closed group was tried on noninvasive ventilation prior to intubation according to our study.According to the five systemic reviews done on noninvasive ventilation,it was found that noninvasive ventilation reduces the intubation rate and mortality,with the greatest benefit being in cases of exacerbations of chronic obstructive pulmonary disease(45, 93-96).A prospective survey(97) which was done in 42 intensive care units for a duration of 3 weeks found that Noninvasive ventilation was used in 16% of mechanically ventilated patients as first-line therapy. Endotracheal intubation was eventually performed in 40% of patients receiving intubation (ie, a 60% success rate).Avoiding intubation obviously prevents ventilator associated pneumonia and the complications associated with intubation. Therefore the option of providing noninvasive ventilation should always be considered prior to initiating invasive ventilation.However the number of patients who were tried on non invasive ventilation were small and should be increased.

The main reasons for admission of patients to the ICU in this study were respiratory or hemodynamic instability or both. Poisoning and drug overdosage constituted 22% of the patients of which majority(19%) were admitted with organophosphorous poisoning.

VENTILATOR ASSOCIATED PNEUMONIA.

There was no difference between closed and open suction groups with regard to VAP. However when the clinical criteria as per the American thoracic Society guidelines was used there was a trend towards a

significant difference(P value 0.06).This finding of no difference in VAP rates is in keeping with the earlier metaanalysis done in other countries(13,92)).

The incidence of ventilator associated pneumonia according to this study was 23.5% taking only clinical criteria and 14% taking into account both clinical criteria and CPIS score. Previous unpublished studies, done prior to three years in the medical ICU of this hospital, had shown the incidence of VAP to be 17%(Dr Cherian R,personal communication)(102) in 1999 and 7-8.5%(personal communication,Dr.Chacko.B,103, Dr Pichamuthu K ,104) in 2005-2006.However the increase in VAP rates in this study could be attributed to the fact that ,the X-rays were reported by an expert radiologist. Studies from India have reported VAP rates to be 16.7%(105) and 47%(21).VAP rates in this study were comparable to that reported in the systemic analysis done earlier(10, 12-14).

There were no significant differences between open and closed groups in the timing of VAP(ie;early or late VAP).The timing of VAP did not vary between patients who were electively intubated and those who required emergency intubation. Median duration of development of ventilator associated pneumonia was 4 days, similar to other studies(30). Most of the studies done on ventilator associated pneumonia identified gram negative bacteria as the most common organism causing ventilator associated pneumonia(106-108).In our study also, of patients diagnosed with VAP,the endotracheal aspirate culture showed significant growth of Pseudomonas aeruginosa in 63.8%.36.17% of the patients grew Staphylococcus aureus and Klebsiella pneumoniae.

Each closed suction catheter was used for a maximum period of one week. Trials elsewhere have shown that prolonged use of CSS(closed suctioning system) was associated with increased microbial colonization of the device(22) without raising the incidence of VAP (98-100) and was considered safe and cost-effective(22, 98-100).Also a survey done among 27 ICUs in the United States revealed that CSS devices were changed every 72 hrs, "as needed," or weekly in 37% of ICUs (101), with no negative effects mentioned. Hence in our study the closed suction catheter was used for a maximum duration of one week

Previous studies have shown that in early onset VAP (<5 days), methicillin-sensitive S.aureus, Streptococcus pneumoniae, and Haemophilus influenzae are the most common pathogens, whereas methicillin-resistant S. aureus (MRSA), P. aeruginosa, Acinetobacter baumannii and Stenotrophomonas maltophilia are more frequent in late onset VAP (≥5 days)(108-110).However, Pseudomonas aeruginosa emerged as the most common isolate in both early onset and late onset pneumonia in our study.Earlier studies(102, 103) done in this hospital also showed Pseudomonas aeruginosa to be the most common organism(35.5%)(103) associated with VAP, followed by MRSA(7.2%)(103)(methicillin resistant Staphylococcus aureus).

MORTALITY

In our study the crude mortality rates were 40% in patients who developed VAP. . No difference was established with respect to mortality or length of stay in ICU or hospital between the two groups.Patients with VAP have a significantly higher morbidity and mortality(28, 37, 111). Heyland et al.(37) reported the crude mortality rate of VAP as 23.7%. In another study, the crude mortality rates for VAP cases

was 65.0% and they found that the mortality rates were highest in high risk pathogens(30). Previous studies done in this hospital showed a mortality rate of 61%(103) in patients with VAP The randomized control trials comparing the open and closed suction also did not find any difference between open and closed groups with respect to mortality or length of stay(45, 92).Though the above trials showed that the duration of mechanical ventilation was significantly lower in open endotracheal suction group,our study did not show any significant difference between the two groups(Open group-6 days,Closed group 5 days,P value-0.651).

LEFT BASAL COLLAPSE

This study found a statistically significant difference in the development of left basal collapse between open and closed suctioning systems favouring closed Open suctioning involves disconnection of ventilator from the endotracheal tube. Disconnection itself can result in airway pressure drop and loss of lung volume,but a further volume decrease is observed during suctioning(82) due to the generation of negative pressure in the airway.One of the disadvantages of closed suctioning systems which has been cited, is the risk of producing high negative pressures during the suction much more than that which is produced with open suctioning system(19).Due to the above reasons we looked at the left basal collapse in open and closed groups..The mean duration of developing collapse was 3.69days(SD- 2.469).We are unable to explain this increase in the open group,but there is definitely no increase of basal collapse in the closed group.

SUCTION-COST AND RELATED ISSUES.

In our study that number needed to treat was 12.5 patients on a closed suction catheter to prevent one ventilator associated pneumonia though the difference was not statistically significant at a P value of 0.05. Considering that the number needed to treat to prevent one ventilator associated pneumonia is 12.5 patients with closed suction catheter,and that the mean duration of ventilation is 6 days with additional cost of suction in closed group being 81.7 Rs per day compared to open group,the total cost for preventing one ventilator associated pneumonia would be 10490.2 Rs. If a patient developes VAP,the common antibiotics used in our ICU are Inj.Piperacillin Tazobactem or Inj.Meropenem which for a duration of 10 days would cost 23640 to 47370 Rs respectively.This cost would cover only the antibiotic cost and does not cover the cost of increased hospital stay and for other morbidity related costs associated with VAP,which when considered would increase the cost much more for a patient with VAP. Hence taking into account the cost involved in treating a ventilator associated pneumonia,the use of closed suction catheter should definitely be considered in all ventilated patients,though a larger study needs to be done to prove the difference statistically before this can be made a standard of care.

In a developing country like India,one of the most important factors considered prior to implementation of a new intervention,especially when there are no clinically proven benefits, is cost effectiveness.Studies done in the west have not given any clear answer regarding the cost difference between the two suctioning systems.Two of the studies(21, 112) have reported higher costs for the closed suctioning system while others(17) have reported lower costs for the same.One study(28) showed that when length of mechanical ventilation was lower than 4 days, the cost was higher

with CTSS than with OTSS (7.2±4.7 Euros vs 1.9±0.6 Euros; $p<0.001$); and when length of mechanical ventilation was higher than 4days, the cost was lower with CTSS than with OTSS (1.6±2.8 Euros vs 2.5±0.5 Euros; $p<0.001$). Our study showed that there was Rs.82 difference in the median cost of suction per day between the two groups.

SUCTIONING TIME AND THE HEMODYNAMIC PARAMETERS.

Our study did not show any significant changes in the arterial saturation between the two suctioning groups. The mean differences in the blood pressure and heart rate change between the two suctioning systems were small and no conclusions could be drawn from the results. However studies(13) have shown significant changes of the above parameters between the CSS and OSS favouring closed suction. This difference could be due to the small sample size in our study and hence further studies would be needed to assess the same.

LIMITATIONS.

1) Baseline charecteristics showed significant difference between the two groups with respect to ischaemic heart disease. However it is not likely to have affected the outcome as no studies have shown increased or decreased VAP with IHD.
2) Patients who got randomized included those who were intubated in the wards and then shifted into medical ICU. Though most patients were shifted within 3-4 hours,there were a subset in whom open suction would have been used in the wards before randomization.
3) Haemodynamic parameters in relation to suctioning could not be assessed for all patients included in the study due to operational reasons.
4) Costing only looked at the suction costs and did not include indirect costs like nursing time,among others.

CONCLUSIONS

In this randomized control trial 200 patients were included and they were randomized into two arms,closed endotracheal suction and open endotracheal suction.

1) The incidence of ventilator associated pneumonia was 23.5% if only clinical criteriae was used for the diagnosis and 14% taking into account both clinical criteriae and CPIS score.
2) There was no difference between the Closed and Open suction groups with regards to the incidence of ventilator associated pneumonias. However ,there was a trend towards a difference in two groups with regard to ventilator associated pneumonia favoring closed suction when clinical criteria as proposed by the American thoracic society guidelines was used. However, considering more stringent criteria(Clinical criteria + CPIS score) to diagnose VAP,this trend was not seen.Late VAP was significantly more in open group(P value 0.03) than the closed group
3) The mortality,duration of stay in ICU or hospital and the duration of ventilation was not significantly different between the two groups.
4) Surprisingly the incidence of left basal collapse was significantly more in the open suctioning system compared to the closed suction.

5) The cost of suctioning per day was 211Rs in the open group and 293Rs in the closed group.
6) The additional direct cost incurred to prevent one VAP by using the closed suction was 10490.2Rs while the cost of treating one VAP in our ICU is 23640 to 47370 Rs.
7) The study did not find any difference between the two groups with regard to the suctioning time and the Hemodynamic parameters.

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ANNEXURE I

Temperature (°C)
> or equal to 36.5 and < or equal to 38.4 = 0 point
> or equal to 38.5 and < or equal to 38.9 = 1 point
> or equal to 39 and < or equal to 36 = 2 points
Blood leukocytes, mm³
> or equal to 4,000 and < or equal to 11,000 = 0 point
< 4,000 or > 11,000 = 1 point + band forms > equal to 50% = add 1 point
Tracheal secretions
Absence of tracheal secretions = 0 point
Presence of nonpurulent tracheal secretions = 1 point
Presence of purulent tracheal secretions = 2 points
Oxygenation: PaO_2/FIO_2, mmHg
> 240 or ARDS (ARDS defined as PaO_2/FIO_2 , < or equal to 200, pulmonary arterial wedge pressure < or equal to 18 mm Hg and acute bilateral infiltrates) = 0 point
< or equal to 240 and no ARDS = 2 points
Pulmonary radiography
No infiltrate = 0 point
Diffuse (or patchy) infiltrate = 1 point
Localized infiltrate = 2 points
Progression of pulmonary infiltrate
No radiographic progression = 0 point
Radiographic progression (after CHF and ARDS excluded) = 2 points
Culture of tracheal aspirate
Pathogenic bacteria cultured in rare or light quantity or growth = 0 point
Pathogenic bacteria cultured in moderate or heavy quantity = 1 point
Same pathogenic bacteria seen on Gram stain, add 1 point

ARDS = acute respiratory distress syndrome; CHF = congestive heart failure; PaO_2/FIO_2 = ratio of arterial oxygen pressure to fraction of inspired oxygen.

* Modified from Pugin *et al.*[15] and by Singh *et al.* [19]

A score > 6 is considered suggestive of pneumonia.

Clinical pulmonary infection score

ANNEXURE II

Data abstraction form – Suctioning study	**PATIENT STUDY NUMBER**	

OPEN SUCTIONING / CLOSED SUCTIONING

Patient name: Hospital number:
Date of birth: ICU number:
ICU Admission: ICU discharge:
APACHE II score: SAPS:

Circle primary reason for ICU admission ⇒

Respiratory failure	**Hemodynamic support**	**Neurologic**	**Monitoring**	**Poisoning**

Intubation status: Previous hospital / E.D / Wards / On ICU arrival / During ICU stay
Lag time from admission to intubation: (hours) Emergency intubn. / Elective intubn.
Prior/subsequent NIV: Yes / No Duration of NIV: _____hours

Co-morbidities ⇒

Diabetes type 1	Diabetes type 2	Hypertension	Hypercholesterolemia
IHD	PVD	Previous CVA	COPD
Current smoker	Ex-smoker	Other Resp. disease	Current Mg
Chronic liver disease	Chronic renal failure	HIV	Previous Mg

Meds ⇒

Steroids	Aspirin	Statins	PPI
Immunosuppressive	HART	Others (list)	
Antibiotics (list names and duration at time of recruitment			

VAP diagnosed: Yes / No Early VAP / Late VAP **Time from MV to VAP (days):**

VAP diagnosis

CLINICAL CRITERIA FULFILLED: YES / NO
CPIS SCORE (BASELINE) _____ SCORE AT 72 HOURS _____

Organisms grown (With CFU & sensitivity)
(1)
(2)
(3)

Antibiotic changed for VAP: Yes / No New antibiotics:
Duration of therapy:

COSTS

Day	1	2	3	4	5	6	7	8	9	10
No of suctions										
Cost of catheter										
Cost of glove										
Total cost/d										

Day	11	12	13	14	15	16	17	18	19	20
No of suctions										
Cost of catheter										
Cost of glove										
Total cost/d										

Total suction cost for entire ventilation: Cost of suctioning/day: Rs.Left basal collapse; Yes / No
If Yes, day developed post intubation: Day resolved:

Duration of ICU stay: _____ hours Duration of hospital stay: _____days
Duration of ventilation: _____ hours

ICU outcome: Died / Alive / Discharged at request Hospital outcome: Died/Alive/Request

Sats

STUDY

Date							
Start time							
Finish time							
Duration (sec)							
Start SaO2							
Finish SaO2							
Start HR							
Finish HR							
Start MAP							
Finish MAP							

Clinical score

YES

NO

New and persistent radiographic infiltrate: Present / Absent, If present need at least 2 to Δ VAP

Temperature	>38ºC or <36ºC (without obvious extra pulmonary infection)	
WBC count	>10, 000 or < 4000	
Purulent tracheal aspirate	Present	
Culture (>1000 CFU)	Present	
Antibiotic change after culture report	Yes	

CPIS Baseline score

TOTAL SCORE

Points	0	1	2
Temperature	**≥ 36.5 and ≤ 38.4**	**≥ 38.5 and ≤ 38.9**	**≥ 39 and ≤ 36**
P/F ratio	**240 or ARDS**		**≤240 and no ARDS**
X-ray patch	**No infiltrate**	**Diffuse (or patchy) infiltrate**	**Localised infiltrate**
Total count	**≥ 4000 and ≤ 11000**	**< 4000 or > 11000**	**< 4000 or > 11000 + band forms ≥ 50%**
Purulent secretions	**Absence of tracheal secretions**	**Presence of non-purulent tracheal secretions**	**Presence of purulent tracheal secretions**

CPIS 72 hours

TOTAL SCORE

Temperature	**≥ 36.5 and ≤ 38.4**	**≥ 38.5 and ≤ 38.9**	**≥ 39 and ≤ 36**
P/F ratio	**240 or ARDS**		**≤240 and no ARDS**
X-ray patch	**No infiltrate**	**Diffuse (or patchy) infiltrate**	**Localised infiltrate**
Total count	**≥ 4000 and ≤ 11000**	**< 4000 or > 11000**	**< 4000 or > 11000 + band forms ≥ 50%**
Purulent secretions	**Absence of tracheal secretions**	**Presence of non-purulent tracheal secretions**	**Presence of purulent tracheal secretions**
Progression of X-ray patch	**No progression**		**Progression (after CHF/ARDS excluded)**
Culture of tracheal aspirate	**Pathogenic bacteria cultured in rare or light quantity or no growth**	**Pathogenic bacteria cultured in moderate or heavy quantity**	**Pathogenic bacteria cultured in moderate or heavy quantity + Same pathogen seen on Gram stain**

APPENDIX III

CONSENT FORM:

INFORMATION TO THE PATIENT

A patient in the ICU on the ventilator needs frequent suctioning of the endotracheal tube to remove collected secretions. This can be done in two ways. One method is using the open suction which requires the patient to be disconnected from the ventilator during that period. This has several disadvantages like possible hypoxic attacks if prolonged disconnection, increase in heart rate and blood pressure, contamination of the surrounding environment and exposure to contaminants in the environment. This may lead to increase incidence of ventilator associated pneumonias (VAP) .The other method is using the closed suction during which the patient need not be disconnected from the ventilator, thus avoiding the above mentioned problems. However, the efficacy of one over the other has not been proved in studies done in developed countries.

This study is being done to determine the difference in incidence of VAP with the usage of both types of suctioning, considering the differences in the ICU settings in developed and developing countries.

If you volunteer for the study your patient would be randomly put into two groups to receive either closed or open endotracheal suctioning.

This study is purely voluntary. You may withdraw from it at any point in time. The care provided to your patient will not be affected by it.

PATIENT CONSENT SHEET

I,_____, _____ of _____

am well aware that my relative is included in the study "Difference in incidence of ventilator assosciated pneumonia with respect to use of open and closed suction catheters in patients admitted to the Medical ICU and that the data collected can be used for publication purposes. I am willing for the same.

Signed _____Relationship with the patient _____

Witness _____Researcher _____

Date _____

In case of any queries:contact Dr.Deepu David,Medicine Registrar,CMCH.Phone No:2282178.

ANNEXURE IV

APACHE II SCORING SYSTEM *

	PHYSIOLOGIC VARIABLE †	POINT SCORE								
		+4	+3	+2	+1	0	+1	+2	+3	+4
1	Temperature, core (°C)	≥ 41°	39-40.9°	—	38.5-38.9°	36-38.4°	34-35.9°	32-33.9°	30-31.9°	≤ 29.9°
2	Mean arterial pressure (mm Hg)	≥160	130-159	110-129	—	70-109	—	50-69	—	≤ 49
3	Heart rate	≥180	140-179	110-139	—	70-109	—	55-69	40-54	≤ 39
4	Respiratory rate (non-ventilated or ventilated)	≥ 50	35-49	—	25-34	12-24	10-11	6-9	—	≤ 5
5	Oxygenation: a) FIO_2 ≥ 0.5: use A-aDO_2	≥ 500	350-499	200-349	—	< 200	—	—	—	—
	b) FIO_2 < 0.5: use PaO_2	—	—	—	—	> 70	61-70	—	55-60	< 55
6	Arterial pH	≥ 7.7	7.6-7.69	—	7.5-7.59	7.33-7.49	—	7.25-7.32	7.15-7.24	< 7.15
7	Serum Na (mMol/L)	≥ 180	160-179	155-159	150-154	130-149	—	120-129	111-119	≤ 110
8	Serum K (mMol/L)	≥ 7	6-6.9	—	5.5-5.9	3.5-5.4	3-3.4	2.5-2.9	—	< 2.5
9	Serum creatinine (mg/dL); double point score for **acute** renal failure	≥ 3.5	2-3.4	1.5-1.9	—	0.6-1.4	—	< 0.6	—	—
10	Hct (%)	≥ 60	—	50-59.9	46-49.9	30-45.9	—	20-29.9	—	< 20
11	WBC (in 1000s)	≥ 40	—	20-39.9	15-19.9	3-14.9	—	1-2.9	—	< 1
12	Glasgow coma score (GCS)	Score = 15 minus actual GCS								

Acute physiology score is the sum of the 12 individual variable points.
Add 0 points for age < 44; 2 points, 45-54 yr; 3 points, 55-64 yr; 5 points, 65-74 yr; 6 points ≥ 75 yr.
Add chronic health status points: 2 points if elective postoperative patient with immunocompromise or history of severe organ insufficiency; 5 points for nonoperative patient or emergency postoperative patient with immunocompromise or severe organ insufficiency. ‡

(13)§	Serum HCO_3 (venous-mMol/L) use only if no ABGs	≥ 52	41-51.9	—	32-40.9	22-31.9	—	18-21.9	15-17.9	< 15

* APACHE II Score = acute physiology score + age points + chronic health points. Minimum score = 0; maximum score = 71. Increasing score is associated with increasing risk of hospital death.

† Choose worst value in the past 24 h.

‡ Chronic health status: Organ insufficiency (eg, hepatic, cardiovascular, renal, pulmonary) or immunocompromised state must have preceded current admission.

§ Optional variable; use only if no ABGs.

Adapted from Knaus WA, Draper EA, Wagner DP, Zimmerman JE: APACHE II: A severity of disease classification system. *Critical Care Medicine* 13:818-829, 1985.